

CROWDSOURCING ANALYSIS OF OFF-LABEL INTERVENTION USAGE IN AMYOTROPHIC LATERAL SCLERSOSIS

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LIST OF ABBREVIATIONS

<u>Abbreviation</u>	<u>Stands For</u>
ALS	amyotrophic lateral sclerosis
AUC	area under the curve
IRB	institutional review board
PCA	principal component analysis

SUMMARY

Background

Amyotrophic Lateral Sclerosis is a neurodegenerative disease resulting in death within 3-5 years. Only riluzole is widely prescribed by clinicians to target the ALS etiology. Most interventions prescribed are “off-label”, meaning they were not developed for ALS, but are used to treat ALS or co-morbid symptoms. We examine relationships between intervention usage, disease duration, and sub-population characteristics (onset age, onset type, gender).

Methods

A form of physician crowdsourcing was utilized to examine intervention usage in a retrospective cohort of 1,585 ALS patients. Data was compiled on a per-visit and per-patient basis.

Interventions were aggregated by active ingredient or indication. Principal component analysis (PCA), Fisher exact test, Kaplan Meir, and conditional random forest were used to determine the significance of relationships between patient characteristics, intervention usage, and disease duration.

Results

A total of 4,168 individual interventions and 564 intervention categories were identified in the cohort. A total 54 intervention categories met the threshold for statistical assessment (e.g. >8.5% usage prevalence); 19 corresponded to statistically significant ($p < 0.05$) increases in disease duration ranging from +4.5-6.5 months. Interventions identified by random forest as the strongest predictors of disease duration (all $p < 0.01$), are: vitamin A (+8.9 months), multivitamin (+8.2 months), feeding tube (+15.5 months), alternative herbal supplements (+9.7 months), antihistamines (+8.4 months), muscle relaxants (+13.4 months), stimulant laxatives (+7.1 months), anti-spasticity (+16.4 months). Usage of anti-cholinergic, anti-depressant, and non-

opioid pain medication also resulted in a statistically significant ($p < 0.05$) increase in survival duration (+6.2, +16.4 months, and +15.2 months, respectively). Riluzole, used by 60% of the cohort, increased disease duration by 1.3 months, albeit insignificantly ($p > 0.05$). No interventions resulted in a significant decrease in survival duration. Female patients used more interventions than males, but gender was not an independent predictor of survival.

Conclusions

We found many “off-label” interventions perform better than the ALS-specific drug, riluzole. Our findings illustrate the complexity of variables contributing to ALS disease duration. Multiple interventions that increase overall health and quality of life, irrespective of whether they specifically target ALS etiology, profoundly increase survival duration likely by boosting “will to live”.

Keywords

ALS, amyotrophic lateral sclerosis, medication list, disease duration, random forest

CHAPTER 1

PHILOSOPHY

The goal of this thesis is to give ALS physicians and patients objectively determined information (using quantitative data analytics) regarding off-label interventions. That is, which interventions are beneficial or could extend the patients' survival duration versus which interventions are likely to shorten disease duration, and thus, should be contraindicated for ALS patients? Every medication that ALS patients take for their symptoms, except for riluzole (brand name Rilutek), is taken "off-label," meaning that the drug was not approved or manufactured specifically for ALS. As such, none of the off-label medications have been tested in an ALS patient cohort. To date, there has not been a comprehensive prospective or retrospective ALS study to evaluate off-label intervention usage, including potential benefits or risks to survival duration.

Crowdsourcing has been successful in amyotrophic lateral sclerosis (ALS) research before, namely the recent Phil Bowen Prize4Life Challenge, to find a computer algorithm to predict ALS progression. This attempt to use crowdsourcing in ALS research involved a competition in which the first 3 months of a patient's data was provided to researchers and the "crowd" was asked to develop an algorithm to predict disease duration [51]. Much of the data from the competition is no longer available, but the top results from the crowdsource predicted the duration of the disease better than the leading expert [51]. PatientsLikeMe in cooperation with Prize4Life, Sage Bionetworks and the DREAM community, sponsored another competition seeking the same or similar results with respect to identifying a genetic or disease difference that may be extending the lives of ALS patients from 2 to 3 years to longer than a decade. A marker that seemed to help with this prediction was found, and three groups were considered the

“winners” of the competition. Thus, there are two recorded occasions of crowdsourcing producing positive results in the acquiring knowledge about ALS [52].

Medical crowdsourcing has been rapidly growing as medical “big data” becomes more accessible to researchers. When it comes to medical crowdsourcing,

The current focus [is] on personal and family health history, prescription records, and current diagnosis and treatment details could be expanded to include predictive risk-assessment modules at the front-end to facilitate the practice of preventive medicine by integrating the relevant health information streams. . . . Crowdsourced health studies and quantified self-experimentation projects conducted individually and in groups are emerging as an important complement to traditional clinical trials and other established mechanisms of health knowledge generation [14].

This study fits into the “health study project as a complement to traditional clinical trials” group. We utilize a non-traditional form of crowdsourcing to assess the usage prevalence of off-label interventions and their relationships to survival duration. In this case, the “crowd” is the host of physicians, most of them general or family physicians, who prescribed the off-label interventions used in this retrospective cohort. To clarify, although all study patients were seen at the same tertiary ALS clinic, the preponderance of interventions were prescribed by physicians outside the specialty ALS Clinic. All interventions, regardless of whether they were internally or externally recommended or prescribed, were transcribed from tertiary ALS clinic records using our lab’s stringent protocols.

We utilize methods of big data analytics to identify interventions that could confer survival benefit, albeit even if they were not specifically intended for ALS. Additionally, we examined literature-cited controversial interventions that have been hypothesized to negatively impact ALS patients. This study utilizes the largest cohort size to date (1,585 patients) to discriminate between recommend interventions versus contraindicated interventions for the ALS population.

CHAPTER 2

CROWDSOURCING OFF-LABEL MEDICATIONS TO EXTEND ALS DISEASE DURATION

Introduction

Amyotrophic lateral sclerosis (ALS) is a neurological disease that causes the death of motor neurons in the central nervous system [1]. This progressive disease typically leads to death in three to five years, although a smaller percentage of patients live ten or more years. ALS affects both lower and upper motor neurons in the cerebral cortex, brainstem, and spinal cord, resulting in muscular atrophy, fasciculation, spasticity, dysphagia, and respiratory weakness [1]. ALS has two predominant onset types: limb onset, which initiates with muscular weakness in the extremities tied to spinal motoneuron degeneration; and bulbar onset, which initiates with speech impediments, drooling, and fasciculation of the head and neck due to the destruction of neurons in the corticobulbar area of the brainstem [2]. A small fraction of patients present with an onset type other than bulbar or limb, which may include symptoms such as generalized or respiratory weakness. The exact etiology of ALS is unknown, although it is thought to be a multi-factorial disease with contributions from oxidative stress, inflammation, genetic mutations, and environmental factors [3-4]. Only 10% of ALS patients are thought to have an inherited or familial form of the disease [5-7]. The incidence of ALS increases with age, and the disease is slightly more prevalent in males than females [8].

Clinical trials to evaluate ALS treatments began in 1939, the same year Lou Gehrig was diagnosed—a famous American baseball player after which ALS was dubbed “Lou Gehrig’s Disease” in the United States. The first clinical trial tested the use of vitamin E, an antioxidant

[1]. Subsequent ALS intervention studies have largely focused on the efficacy of nutritional supplements [18-21], general exercise [23], and pain medication [24-25], as measures to enhance quality of life. Riluzole (brand name Rilutek), a sodium channel blocker, is the only United States Food and Drug Administration approved treatment explicit to targeting the underlying etiology of ALS, and it remains the only drug consistently used worldwide to directly treat ALS [30]. However, the efficacy of Riluzole is limited; on average, it extends life 1-3 months if treatment is initiated early in the disease course [30].

Much remains unknown about the disease and the best treatments for both enhancing quality of life and increasing disease or survival duration [9]. A major hurdle in identifying ALS interventions has been the degree of heterogeneity in the ALS population, including patient characteristics and survival duration. The amount of variance simply drowns out all but the most extreme effect sizes in clinical trials. Another hurdle is sample size. The prevalence of ALS is much lower than other neurodegenerative diseases like, Alzheimer's Disease. Therefore, ALS has not received as much academic or pharmaceutical research priority, although the 2014 ALS Association Ice Bucket Challenge did bring about worldwide public awareness. Between the heterogeneity in the population and the overall lower prevalence, assessment of therapeutics for ALS has been painstakingly slow and difficult.

Given that Riluzole is the only drug explicitly prescribed for ALS, most of the other drugs used by ALS patients are prescribed by physicians "off-label", meaning the drugs prescribed were not specifically developed or approved for treating ALS. Such off-label interventions are used to treat the symptoms directly caused by ALS (e.g. spasticity, drooling, dysphagia, weight loss, etc.), co-morbid conditions indirectly associated with ALS (e.g. depression, pain), common antecedent or co-morbid conditions typically thought to be unrelated

to ALS (e.g. diabetes, hyperlipidemia, hypertension, etc.), or to maintain overall health (e.g. nutritional supplements, vitamins, etc.).

In the present study, we evaluate the usage prevalence of predominantly off-label interventions prescribed to ALS patients. We assess the interventions' correlations to disease duration and ALS patient characteristics (onset age, onset type, gender) in a 1,585 ALS patient cohort. The overall goal was to identify interventions that are positively contributing to ALS disease duration and differentiate interventions that may be contraindicated. Given that Rilutek is the only ALS-specific intervention, most of the interventions used by patients were originally prescribed by general practice physicians outside a tertiary or specialty ALS clinic. Given that the interventions are prescribed by a host of different physicians, we utilize the concept of “crowdsourcing”, defined as the practice of obtaining needed services, ideas, or content by soliciting contributions from a large group of people [10], to evaluate the impact of intervention usage as a function of patient characteristics and disease duration. Although it has shown remarkable success in business, crowdsourcing is a relatively new technique in medicine [14]. However, it has already proven to be effective in generating more effective treatment paradigms or outcome algorithms [15]. In summary, we assess the complexity and correlations in intervention usage data to draw conclusions that can be used by physicians to establish the benefits and risks of specific off-label interventions in ALS.

Methodology

We perform a retrospective study of a tertiary ALS patient cohort, which includes de-identified and anonymized medical records from 1,585 patients of the Emory ALS Clinic (Emory University Hospital, Atlanta, GA). The patient population (Table 1) included 945 males and 640 females. A total of 558 patients were excluded due to lack of time of death data. Data transcription and quality control is as previously published [31]. Transcribed data was placed in a relational database using Filemaker Pro. Recorded interventions included prescription medications; non-prescription or over-the-counter medications; nutritional supplements; percutaneous endoscopic gastronomy (PEG) or feeding tube; and specialized support (family, home health care, physical therapy, ALS support group, etc.). Recorded temporal and patient characteristics included age, onset age, onset type, gender, and age at time of death. Disease duration was calculated using the onset age and age at time of death. The study received Internal Review Board approval from Georgia Institute of Technology and Emory University.

Intervention categorization

The categorization of interventions was accomplished by first sorting each unique word in the name of the prescription medication, over-the-counter (non-prescription) remedy, durable medical equipment or other supportive intervention. All interventions in the patient's medical record were included, whether specific for treatment of the etiological underpinnings of ALS (e.g. riluzole), adjunctive for ALS-related symptoms (anti-spasticity, anti-drooling medications, percutaneous endoscopic gastronomy or feeding tube), treatment of co-morbid conditions (anti-diabetic, hyperlipidemia, etc.) or for general health (e.g. multi-vitamin, specialized human support). An automated word search was completed for each unique word present in the

transcribed intervention database for the entire patient cohort. Interventions were then grouped by their pharmacological class, active ingredient, or intended purpose [32-34]. If, for example, a medication consisted of two unique drugs in different classes, the medication was assigned to both relevant intervention categories (for example, uniretic is classified as thiazide diuretic and ACE inhibitor). The complete listing can be found in Appendix A. Identification of intervention usage was performed on a per-patient basis and per-visit basis (Tables 2 and 3), with per-patient usage utilized for statistical analysis.

Patient Characteristics Categorization

Included temporal patient characteristics comprise age, age at symptom onset, age at time of death, and onset type. Tiers for ages were created using the statistical mean and standard deviation. A two-tier analysis comprised one group above and one below the mean. A three-tier grouping consisted of one group below the mean reduced by one-half the standard deviation, one group above the mean plus one half the standard deviation, and one group in between the two groups. Lastly, two-tier age groups were made up of one group below and one group above 55 years old. An age of 55 was considered a tier threshold criteria based on its standardized use in the field in prior literature (1). Of the 1,585 patients (Table 1), 418 were identified with bulbar onset, 1078 with limb onset, and 89 as “other” onset (respiratory, general, unknown, or unclassifiable).

Statistical Analysis

Fisher’s exact test was used to find a difference between a 2x2 contingency square to show the exact p-value between two classification data sets.

Principal Component Analysis (PCA) was used to gauge the importance of one variable in predicting another variable, as well as to explain the variance in the data. The PCA components included the following data: 1) intervention categories with greater than 8.5% prevalence of usage within the cohort; 2) patient characteristics associated with the corresponding interventions with greater than 8.5% prevalence of usage within the cohort. The threshold of 8.5% was chosen based on statistical power. PCA results are visualized using a biplot, which maps the two PCA components best explaining variance. Variables are mapped onto the two dimensional biplot in the form of vectors. The lengths of the vectors are proportional to the weightings of the variables explaining the variance; the angles between a pair of vectors are proportional to the covariances, and the sign of the vectors signify a relationship between the variable and the principal component.

Random Forest modeling, a type of machine learning algorithm, was used to identify and quantify connections between intervention category usage and patient characteristics. The data used in this study, however, was not easily evaluated by traditional random forest analysis. To address potential class imbalances in the data [35], we utilized a less biased method of random forest known as conditional random forest [36-37]. The conditional forest model was run four times and the variable importance was averaged into one plot as shown in Appendix D. The area under the curve (AUC) version of variable importance was used as the performance metric, as it provides more reliable results with unbalanced data [38-39].

Results

Database Overview

Table 1 summarizes the study population, including number of patient visits, ALS onset age, disease duration, and ALS onset type. The 1,077 limb patients have an average ALS onset age of 58.54-years at onset and a disease duration of 4.04-years, whereas, the 418 bulbar patients present have an average ALS onset age of 63.99 onset and a disease duration of 2.88-years, which is consistent with prior literature [11].

Specific and categorical intervention usage

Table 2 shows the individual or specific interventions and their prevalence of usage by ALS patients (i.e. percent of patients using the intervention). Rilutek, the only ALS-specific drug, was taken by nearly 60% of the patients. Other common interventions include, vitamin or multivitamin (41%); baclofen (14%); aspirin (10%); and clonazepam (6%). Table 3 defines the aggregate intervention categories utilized for in-depth analysis. Individual interventions are grouped by their intended effect or ingredient and encompass usage by greater than 15% of the cohort. While not a drug, “support” (e.g. family, social, mental healthcare, support group, etc.) was used as an intervention in over 61% of ALS patients. Other commonly used interventions shown in Table 3 include NSAIDs (for mild to moderate pain or inflammation), stimulants (for energy or to increase the rate of physiological processes), nutritional supplements (to maintain weight), vitamins (for general health), SSRIs (for depression), and opioids (for acute or intense chronic pain). Figure 1, a Chinese-hand fan shape commonly used to depict correlations in

genomics, provides a visual representation of patient intervention usage. The usage prevalence is represented by the size of the connection bar for each intervention category.

Complexity between patient characteristics and intervention usage

Figure 2 demonstrates the complexity of the data set. There are 18 principal components (determined from PCA) that contribute to the variance explained by the 54 intervention categories, which are utilized by at least 8.5% of the population. Dimensional reduction (18 components explaining the corresponding variance of 54 interventions) is standard in biology and medicine. In the present context, dimensional restriction corresponds to degeneracy, or correlational overlap, being informationally imparted on the assessed outcome (i.e. survival).

Figure 3 visualizes the two biplot planes that make up over 17% of the variance in the dataset. In these two planes, it is apparent the x-axis sufficiently distinguishes intervention categories from disease characteristic categories, with the exception of disease duration. If two interventions have the same angle, such as acetaminophen and feeding tube, it indicates that the covariances on the component are the same, but the standard deviation is different (e.g. standard deviation of acetaminophen is less than that of the feeding tube). However, if intervention vectors have the same magnitude, like ICI and statins, it indicates the covariances on the component are different, but the standard deviation of the component is the same. The covariance explains how similar the two variables are to each other, while the magnitude explains how much variance each variable explains in context to the larger data set. In addition to the more traditional biplot, the Chinese-hand fan shape (Figure 1) gives a visual representation of which medications have strong covariances with each other. Generally speaking, reading the

Chinese-hand fan shape downwards illustrates the best interventions for prolonging ALS disease duration, which is located at the top of the fan.

In addition to visualizing the covariances and the usage prevalence of each intervention category, Figure 1 specifically shows the connections between intervention usage and ALS patient characteristics. The connections demonstrate the degree that each patient characteristic connects with each intervention. Rilutek, the vitamins, the stimulants, and support have many connections to the other medications. Longer disease duration has more connections than shorter disease duration, in part, because the longer disease duration sub-population dominates the overall data set by a greater than three to one ratio (741 patients to 232 patients), and in part, because patients with longer disease duration tend to use more interventions. Another interesting result is that males and females have roughly the same number of intervention connections despite males outnumbering females roughly three to two. This finding indicates that female patients use more interventions per capita. While a few medications are female-specific, the presence of female-specific interventions (such as progesterone) cannot fully account for the overall higher usage prevalence of multiple simultaneous interventions by females in the patient cohort.

Random Forest includes complex interaction between all variables when determining which variables are most predictive of a specific response variable. In Figure 4, random forest was used to determine which variables are most predictive of onset type (Figure 4A), gender (Figure 4B), and onset age (Figure 4C). Each of the graphs' bars illustrates the area under the curve (AUC) values calculated by random forest; a larger relative AUC indicates the variable is more predictive of the examined response. The classification directly above the bars denotes the ratio of intervention usage among binary sub-populations. For example, the "F" above the bars

in Figure 4B means that female usage (females using the intervention divided by total females in the cohort) is higher than male usage (males using the intervention divided by total males in the cohort). The corresponding statistical significance for intervention categories is calculated from the Fisher exact test and denoted by the markers listed in the figure caption.

Figure 4A examines the relationships between intervention usage and limb or bulbar onset sub-populations. The most predictive intervention category is anticholinergics, an intervention category predominantly used to treat excessive drooling, especially in bulbar ALS patients ($p < 0.001$). Despite being predominantly used by bulbar onset patients, which generally have a shorter disease duration compared to limb onset patients, anticholinergics nonetheless confer a positive increase in average overall disease duration. In fact, patients taking anticholinergics had an overall average disease duration of 4.12 years. When disease duration for anticholinergics usage was examined by onset type sub-population, bulbar and limb patients had a mean disease duration of 3.62 and 4.52 years, respectively. Both of these were substantial improvements from the average ALS patient disease duration of 2.88 years for bulbar onset and 4.04 years for limb onset.

Figure 4B examines the relationships between interventions usage and gender sub-populations. The general hypothyroidism category was the most important variable in the gender random forest model. Levothyroxine usage, a treatment for hypothyroidism, was second for predicting gender (in this case, female). The 3:1 ratio of females to males using hypothyroidism interventions is actually low compared to the general population where women are 5-8 times more likely than men to be treated for hypothyroidism.

In Figure 4C the random forest results for ALS onset age are shown. Disease duration is the most predictive variable with a 3:2 ratio between it and the next most important predictor,

anti-spasticity intervention usage. The fact that disease duration is more important to the model than usage of any intervention illustrates the dominance of age in predicting disease duration. The high significance of the anti-spasticity intervention ($p < 0.001$) aligns with large age gap between anti-spasticity intervention users. The mean onset age for the 340 patients using anti-spasticity interventions was 54.5 years whereas the mean onset age of the 1,245 patients not using anti-spasticity medication was 61.8 years. Although it may be hypothesized that anti-spasticity interventions would be used predominantly by limb onset, interesting, the usage of anti-spasticity interventions was not a predictor of onset type, as illustrated by its absence in Figure 4A. Thus, in this cohort, the connection of anti-spasticity usage with onset age is not attributed to a co-correlation with onset type.

Fisher's exact test analysis of disease duration

Of the 54 intervention categories, 19 categories were found to correspond to a significant change in disease duration ($p < 0.05$) ranging from 4.5 months (e.g. sedatives, $p < 0.01$) to 16.5 months (e.g. anti-spasticity, $p < 0.01$). No intervention was found to result in a statistically significant decrease in disease duration ($p < 0.05$). Four interventions had extremely significant increases ($p < 0.001$) in disease duration, including feeding tube (+15.5 months), alternative herbal medicines (+9.6 months), Vitamin A (+8.9 months), and multivitamins (+8.2 months).

Of the 19 interventions found to statistically increase disease duration, only 7 interventions were found to have a significantly higher usage prevalence ($p < 0.05$) on the basis of onset age; all 7 such categories (anti-spasticity, muscle relaxant, sedative, feeding tube, vitamin E, tricyclic antidepressant, antinuclear antibody, nutritional supplement, and anticonvulsant) are more prevalently utilized by the younger onset age group (onset age < 55 years). Nine of the 19

interventions that statistically increased disease duration had a statistically higher usage prevalence ($p < 0.05$) on the basis of gender; all 9 categories (stimulant, stimulant laxative, nutritional supplement, antihistamine, vitamin, non-opioid pain management, antinuclear antibody, anticholinergic, and muscle relaxants) were more prevalently utilized by females than males. Finally, 5 of the 19 interventions that statistically increased disease duration had a statistically higher usage prevalence ($p < 0.05$) on the basis of onset type. Four interventions were more prevalently used by limb onset (muscle relaxant, anti-spastic, vitamin A, vitamin) whereas one intervention was more prevalently used by bulbar onset (anti-cholinergic).

For comparison, riluzole (the only ALS-specific drug) was found to increase disease duration by 1.3 months; while this was not found to be a statistically significant increase ($p > 0.05$) in the present cohort, the extended disease duration seen with riluzole was comparable to previous studies [31]. Riluzole did have a significantly greater usage by males than females ($p < 0.01$); significantly greater usage ($p < 0.001$) in the onset age < 55 years population compared to onset age > 55 years; and no statistically significant difference ($p > 0.05$) in usage between limb or bulbar onset.

Kaplan-Meier analysis of disease duration

Kaplan Meir analysis was used to visualize trends of probability of survival since ALS onset. Figure 5 shows the Kaplan-Meier plots for ALS sub-populations in the study cohort. Figure 5A illustrates the overall probability of survival trends.

Figure 5B illustrates intervention-specific survival curves. Rilutek and the feeding tube were the two interventions chosen for illustration due to their known ALS indication as well as their large usage prevalence in the cohort. The feeding tube has a discernable difference between

probability of survival of those using the intervention versus not using it; specifically, feeding tubes increase the probability of survival across all disease durations. The differences in probability of survival between users and non-users is not as discriminatory for Rilutek usage, although a weak qualitative trend is evident that illustrates conferred survival benefit for Rilutek users.

Figure 5C shows onset type and onset age. Patients with an onset age <55 years clearly have a better probability of longer survival compared to those with onset at >55 years. Limb onset has the second highest rate of survival duration. Although limb onset survival probability is better than bulbar onset, the collinearity of onset type with onset age (i.e. there is a larger percentage of bulbar onset patients with an onset age >55 years) infers that this is not an independent trend. Thus, once again, onset age tends to dominate the prediction of disease duration as it outweighs the impact of any other patient characteristic or intervention usage category.

Figure 5D shows that gender does not have a clearly discernable trend for survival rate or duration; rather the Kaplan Meir trends for male and females cross each other several times, indicating that gender, alone, is not an independent predictor of disease duration.

Random forest predictors of disease duration

The Fisher's exact test, alone, does not account for complex interactions that influence disease duration; in contrast, random forest modeling does consider the complex interactions contributing the response variable of disease duration. Figure 6 illustrates the relative AUCs of the top variables identified by random forest as the best predictors for determining disease duration. There are three patient characteristic categories and eight intervention categories

shown in the top 11 predictive variables. The collinear onset age and onset type are, unsurprisingly, the top two predictors whereas gender, the least predictive of the patient characteristics, was ranked 11th. The eight in-between predictors of disease duration, respectively ranking 3 through 10, are all intervention categories: vitamin A, multivitamin, feeding tube, alternative herbal medicine, antihistamine, muscle relaxant, stimulant laxative, and anti-spastic interventions. All 8 off-label medications have a higher usage prevalence in the longer disease duration population. In the Fisher exact tests, the significance of these respective interventions were all $p < 0.001$.

Discussion

Promising treatment interventions

This crowdsourcing analysis of predominantly off-label intervention usage in 1,585 ALS patients identifies 19 intervention categories whose usage correlates with a statistically longer disease duration (i.e. longer survival duration). One of the most notable among these is vitamin A, but even multivitamins containing vitamin A also performed well. Additional interventions with a definitive statistically significant impact on disease duration include: feeding tubes, stimulants, anticholinergics, antihistamines, muscle relaxants, stimulant laxatives, anti-spasticity, non-opioid pain medication, antidepressants, and anticholinergics. Others of qualitative positive interest, but with low sample size include, quinine, general breathing medications, iron supplements, and tetracycline antibiotics. Additional analysis with random forest showed that some of the interventions' efficacy correlated more strongly to patient characteristics, such as onset type, onset age, and gender.

This study identified 25 off-label (or non-ALS specific interventions) that perform equal or better than riluzole/Rilutek. Not surprisingly, the only ALS-specific drug, Rilutek (generic name riluzole), was found to have the highest usage prevalence with 60% of ALS patients using the drug in this cohort. On average, riluzole, has been shown to increase disease duration by 1-3 months [9], a result that is qualitatively supported by the present study.

In Figure 4B, a direct comparison of the feeding tubes with Rilutek establishes the superiority of the feeding tubes when comparing the differences in survival length from patients using each intervention. Feeding tubes and nutritional supplements, which counteract the dysphagia in ALS to keep patients at healthy weights, have been previously shown to be

effective in prolonging life in ALS [41-42]. Moreover, usage of Rilutek and feeding tube does not have to be mutually exclusive; these interventions can be used in combination, as can most of the off-label interventions found to prolong life in this study.

Our large, comprehensive study supports findings of other smaller trials identifying the positive effects of vitamins and herbal support in extending survival duration in ALS. Melatonin, an antioxidant, was found to be helpful in ALS mice, and not harmful in humans [40]. It is likely that vitamins are enabling the natural physiological defense and compensatory mechanisms to counteract the oxidative stress and inflammation associated with ALS, thus slowing the rate of motoneuron degeneration.

While low sample size prevents a definitive conclusion, another interesting finding is the qualitative trend of increased diseases duration in ALS patients using iron supplements. Iron is used for maintaining regular metabolic processes, and has been shown to be effective in mouse models [45]. The impact of iron homeostasis in ALS has been a topic in recent years.

Finally, another lesser-used intervention that may provide conferred ALS survival benefit is tetracycline antibiotic, an intervention used by a sub-population in the cohort most likely to combat chronic co-morbid bacterial infections. Other than its bactericidal effects, tetracycline could be particularly helpful as an intervention in ALS due to inhibition of microglial activation, the attenuation of apoptosis and the suppression of reactive oxygen species production. However, this neuroprotective effect in ALS patients does not necessarily apply to all anti-biotics as some other antibiotic classes have shown to be harmful to ALS patients [46].

Interventions for ALS-related symptoms

Most interventions target ALS symptoms (spasticity, drooling, dysphagia, respiratory weakness, etc.) or “side effects” indirectly related to ALS (depression, pain, low energy, etc.), instead of targeting the cellular physiology; such interventions are intended to enhance quality of life. The will to live has been shown to be a crucial factor in increasing survival duration in many intractable or terminal diseases [31]. The present large-scale study supports findings of previous smaller studies indicating the significance of quality of life interventions in increasing survival duration.

Antidepressants are used to combat depression, whether it be directly tied to frontotemporal dementia or other cognitive decline that occurs in about 25% of patients, or for depression simply related to the psychological and emotional weight of the diagnosis, corresponding symptoms, and fear of death. When looking at multiple antidepressant intervention groups, SNRI, SSRI, tricyclic antidepressant, and general antidepressants all had a positive trend with increased disease duration. However, tricyclic anti-depressants were the best performers, increasing disease duration by an impressive 16.4 months ($p < 0.05$). Interestingly, stimulant laxatives and stimulants, which increase physiological activity, also have a positive correlation with increased disease duration (+7 months, $p < 0.01$), that likely corresponds to improved quality of life. Other interventions that increase disease duration, likely through increasing quality of life, are the pain-relieving interventions. Although ALS mostly affects motor versus sensory neurons, many patients report increased pain, which is likely exacerbated by spasticity or inability to move, resulting in stiffness, muscular, and joint pain. Non-opioids outperform opioids, illustrating a statistically significant increase in disease duration ($p < 0.05$, +16.5 months) compared to ($p > 0.05$, +6.5 months). Although pain management is known to improve the quality of life in patients [47], a common concern specifically with opioids and

antidepressants is that they may have an undesired synergistic effect that exacerbates respiratory depression in ALS patients that either already have or are susceptible to respiratory muscle weakness. Based on the findings of the present study, the combination of opioids with antidepressants appears to understandably be highly regulated by physicians; nonetheless, the sub-population that used an antidepressant + opioid combination did, on average, live longer (+12 months for an average duration eclipsing 5 years) than those on opioids alone. Finally, we qualitatively affirm previous literature [31] demonstrating the effectiveness of specialized human or family support; while the effect was not statistically significant ($p>0.05$), the conferred survival benefit was +4.2 months, which was better than riluzole.

Respiratory deficiency, due to partial or complete paralysis of diaphragm and intercostal muscles from ALS, not only decreases quality of life but can also be life-threatening.

Antihistamines, which have not been previously studied in ALS, appear to be very beneficial in extending disease duration in the present study (+8.4 months, $p<0.01$), and ranked as the 5th best intervention in predicting disease duration according to random forest analysis. It is hypothesized that the efficacy of antihistamines is related to airway clearance and enabling easier respiration [43].

Similarly, we show that anti-drooling medications (anticholinergics) significantly extend disease duration in both bulbar and limb patients (+6.2 months, $p<0.05$). Decreasing excessive salivary secretion not only improves quality of life but also decreases risks of associated aspiration in the presence of dysphagia. Of note is that only one anti-drooling medication, glycopyrrolate, was found to be less efficacious. Markedly, almost half of the patients taking anti-drooling interventions also take antidepressants, a finding that suggests a link between drooling and depression. Notably, the patient sub-population using both anti-drooling and anti-

depressant interventions in combination had a longer disease duration than sub-populations using either intervention alone.

Literature-hypothesized “controversial” interventions

There are some interventions that have been shown in previous studies to be contraindicated in ALS due to their relationship with shortened disease duration, namely medications used to treat diabetes, hyperlipidemia (high cholesterol), and hypertension. In the present study, Insulin, which is predominantly used to treat type 1 diabetes correlated with increased disease duration. Metformin, a type 2 diabetes medication that is also used to treat insulin resistance, appeared to decrease disease duration, albeit not significantly. Our examination of cholesterol or hyperlipidemia interventions (commonly used statins and fibrates) was inconclusive. Interestingly, niacin, a B3 vitamin known for its cholesterol-reducing properties, was found to increase disease duration. Our examination of interventions used to treat hypertension, or high blood pressure, showed that ACE inhibitors, beta blockers, and diuretics, were all medication taken almost exclusively by the most vulnerable population for short ALS disease duration, and yet, all of the aforementioned interventions trended with increased disease duration. Only one hypertension medication, the angiotensin ii receptor class, showed a qualitative, albeit insignificant, decrease in disease duration. It is likely that perceived negative relationships of interventions for diabetes, hyperlipidemia, or hypertension with ALS disease duration is intertwined with ALS onset age. These antecedent conditions and their treatment are statistically more prevalent in the onset > 55 years sub-population.

Possibly “negative” interventions

No medication examined in the present study was found to decrease disease duration (i.e. statistically significant shorter survival). However, a few interventions that qualitatively showed a trend towards a decrease in disease duration that should be further evaluated include: thiazide diuretic, norepinephrine reuptake inhibitor (neural uptake reinhibitor with appetite suppression side effect), ondansetron (anti-emetic to treat nausea and vomiting), colchicine (anti-inflammatory medication), and barbiturate (central nervous system depressant). Due to sample size and/or lack of statistical significance, no definitive conclusion can be drawn from this study as to whether or not the aforementioned ‘possibly negative’ interventions should be contraindicated for ALS.

Disease complexity

Recognition of the complexity of ALS as a system-level, multi-factorial disease is important in understanding the difficulty of unraveling specific effects from intervention and patient characteristic categories (gender, onset age, onset type). The x-axis of the biplot (Figure 2A) does well to separate the effects of intervention categories from patient characteristic categories. However, the one key exception is disease duration. Clearly, the primary outcome of ALS, disease duration, is extremely complex. The fact that 54 of the intervention categories plus four disease characteristic categories can only be simplified into 18 components supports this conclusion.

This study affirms that onset age is a crucial predictor of ALS disease duration. Onset type is collinearly related to onset age, and thus, while it can be used as a predictor of disease duration, it is not an independent predictor and is not superior to onset age. Gender was the eleventh predictor (out of 58 total categories) in terms of random forest variable importance in

predicting ALS disease duration. While there are overlapping ties of gender with disease duration, the performance of gender illustrates it is not a primary or independent predictor. In fact, we recommend the effect of gender as a “normalizing threshold” for determining potential significance of the effect of an intervention on ALS disease duration. That is, interventions of either positive or negative interest to ALS should predict disease duration better than gender. Interventions that predict longer survival duration should be considered as ALS therapeutics whereas those that show shorter survival duration should be considered as possibly contraindicated in ALS.

Tables

Table 1: Overview of the ALS Database: All Emory ALS patient data. This includes data on the number of visits, patients, and average disease duration for the data total, male, female, bulbar onset, and limb onset.

	Total	Male	Female	Bulbar	Limb
Patients	1585	945	640	418	1078
Patients with Date of Death	1015	589	426	319	635
Visits	8118	5020	3098	1844	6006
Visits with Date of Death	4629	2781	1848	1226	3238
Age of Onset (years old)	60.21	58.99	62.03	63.99	58.54
Disease Duration (years with ALS from onset to death)	3.67	3.73	3.58	2.88	4.04

Table 2: Overview of top individual medications taken by ALS patients: Most common 50 individual medications taken by patients in the database with how many visits (out of 8118) and patients (out of 1585) that medication was recorded for as well as which intervention categories (total of 564 categories) that medication appeared under. The full list of 4168 medications is Appendix A.

Medication	Appearances in patients	Appearances in Visits	Intervention categories
Rilutek	945 (59.6%)	2874 (35.4%)	ALS treatment
Vitamin	575 (36.3%)	1528 (18.8%)	vitamin
Baclofen	227 (14.3%)	560 (6.9%)	antispastic , muscle relaxant
Aspirin	152 (9.6%)	357 (4.4%)	irreversible cyclooxygenase inhibitor , NSAID
Multivitamin	94 (5.9%)	234 (2.9%)	multivitamin
Clonazepam	89 (5.6%)	219 (2.7%)	benzodiazepine
Glycopyrrolate	80 (5%)	166 (2%)	anticholinergic
Lexapro	79 (5%)	139 (1.7%)	SSRI
Gabapentin	77 (4.9%)	170 (2.1%)	anticonvulsant , antiepileptic
Lisinopril	74 (4.7%)	160 (2%)	ace inhibitor
Lortab	73 (4.6%)	131 (1.6%)	acetaminophen , opioid
Fish	62 (3.9%)	141 (1.7%)	omega 3, nutrient supplement
Calcium	59 (3.7%)	158 (1.9%)	calcium supplement
Cough	58 (3.7%)	104 (1.3%)	general cough
Ambien	57 (3.6%)	96 (1.2%)	sedative
Vitamin E	56 (3.5%)	155 (1.9%)	vitamin e
Topical	56 (3.5%)	134 (1.7%)	skin ointment
Fatty	55 (3.5%)	146 (1.8%)	omega 3
Levothyroxine	54 (3.4%)	131 (1.6%)	levothyroxine
Potassium	54 (3.4%)	114 (1.4%)	potassium
Zoloft	52 (3.3%)	93 (1.1%)	SSRI
Tramadol	51 (3.2%)	102 (1.3%)	analgesic
Albuterol	49 (3.1%)	120 (1.5%)	bronchodilator
Xanax	49 (3.1%)	105 (1.3%)	benzodiazepine
Docusate	49 (3.1%)	91 (1.1%)	stool softener
Ibuprofen	48 (3%)	133 (1.6%)	NSAID
Coenzyme	48 (3%)	95 (1.2%)	coq10
Zolpidem	48 (3%)	94 (1.2%)	general sleep
Polyunsaturated	47 (3%)	130 (1.6%)	good fat
Metoprolol	47 (3%)	96 (1.2%)	beta blocker
Robinul	47 (3%)	71 (0.9%)	general ulcer prevention
Quinine	45 (2.8%)	82 (1%)	quinine
Hydrochlorothiazide	44 (2.8%)	91 (1.1%)	potassium-sparing diuretic , thiazide diuretic

Paxil	44 (2.8%)	87 (1.1%)	SSRI
Prednisone	44 (2.8%)	87 (1.1%)	corticosteroid
Klonopin	44 (2.8%)	63 (0.8%)	benzodiazepine
Tizanidine	43 (2.7%)	96 (1.2%)	muscle relaxant
Citalopram	42 (2.6%)	138 (1.7%)	SSRI
Magnesium	42 (2.6%)	92 (1.1%)	magnesium
Lorazepam	42 (2.6%)	74 (0.9%)	benzodiazepine
Omeprazole	41 (2.6%)	77 (0.9%)	general gastro , proton pump inhibitor
Amitriptyline	40 (2.5%)	105 (1.3%)	tricyclic antidepressant
Simvastatin	40 (2.5%)	99 (1.2%)	statin
Alprazolam	39 (2.5%)	92 (1.1%)	benzodiazepine
Synthroid	38 (2.4%)	63 (0.8%)	levothyroxine
Oil	37 (2.3%)	93 (1.1%)	omega 3 , alternative herbal medicine
SI	36 (2.3%)	78 (1%)	sublingual
Nexium	36 (2.3%)	75 (0.9%)	proton pump inhibitor
Enteral	36 (2.3%)	63 (0.8%)	feeding tube
Trazodone	35 (2.2%)	92 (1.1%)	trazodone

Table 3: Overview of top intervention categories taken by ALS patients: The most common intervention categories (making up more than 15% of patients) in the database with how many visits (out of 8118) and patients (out of 1585) that intervention was recorded for as well as which a definition of the intervention categories and example of interventions that appear in this category. Appendix B has every 564 intervention category as well as additionally a mark if the intervention category falls under usage by 8.5% of the ALS population.

Intervention Category (Code)	Appearances in Patients (% of 1585)	Appearances in Visits (% of 8118)	Definition of Category	Examples of Medications
Support (Suppt)	972 (61.3%)	2722 (33.5%)	Any medical attention that comes directly from another human	PT, Visit, Wife, Hospice
Rilutek (Riluk)	945 (59.6%)	2874 (35.4%)	Glutamate blocker Specifically made to treat amyotrophic lateral sclerosis	Rilutek, otherwise known Riluzole
NSAID (NSAID)	661 (41.7%)	1685 (20.8%)	Provide analgesic and antipyretic effects, and, in higher doses, anti-inflammatory effects	Aspirin, Ibuprofen, Celebrex, ASA
Stimulant (Stimut)	646 (40.8%)	1703 (21%)	Increase activity of the body, drugs that are pleasurable and invigorating, or drugs that have sympathomimetic effects	Nuedexta, Excedrin, Adderall, Methylphenidate
Stimulant laxative (Stimte)	641 (40.4%)	1663 (20.5%)	Induce bowel movements by increasing the contraction of muscles in the intestines, and are effective when used on a short-term basis.	Senna, Bisacodyl, Dulcolax, Senokot
Nutritional Supplement (Nutrlt)	618 (39.0%)	1528 (18.8%)	Foods meant to either maintain or gain weight while providing the vitamins and nutrients needed to live a healthy human life.	IV, Can, Nutrition, Meals
Vitamin (Vitan)	575 (36.3%)	1528 (18.8%)	Intended to be an individual or combination dietary supplement with vitamins, dietary minerals, and other nutritional elements	Vitamin
Calcium Supplement (Calcst)	555 (35.0%)	1464 (18%)	Mineral that is an essential part of bones and teeth. The heart, nerves, and blood-clotting systems also need calcium to work.	Calcium, Caltrate, Citracal, Ca+
SSRI (SSRI)	524 (33.1%)	1494 (18.4%)	Typically used as antidepressants in the treatment of major depressive disorder and anxiety disorders	Lexapro, Zoloft, Paxil, Citalopram
Opioid (Opiod)	516 (32.6%)	1276 (15.7%)	Reduce the sending of pain messages to the brain and reduce feelings of pain	Lortab, Percocet, Hydrocodone, Oxycodone
Vitamin A (VitaA)	488 (30.8%)	1277 (15.7%)	Unsaturated nutritional organic compounds that includes retinol, retinal, retinoic acid, and several provitamin A carotenoids.	Carotene, Betacarotene, Retin, Vita
ACE inhibitor (ACEhr)	469 (29.6%)	1218 (15%)	Heart medications that widen, or dilate, your blood vessels	Lisinopril, Lotrel, Benazepril, Enalapril
Benzodiazepine (Benzae)	440 (27.8%)	1203 (14.8%)	Agents that work on the central nervous system, acting to inhibit or reduce the activity of nerve cells within the brain.	Clonazepam, Xanax, Klonopin, Lorazepam
Potassium-sparing diuretic (Potasd)	422 (26.6%)	1015 (12.5%)	Diuretic drugs, promote diuresis, that is, the increased production of urine, but do not promote the secretion of potassium into the urine.	Hydrochlorothiazide, HCTZ, Spironolactone, Triamterene
Beta blocker (Beta)	394 (24.9%)	1004 (12.4%)	Medications that are particularly used to manage cardiac arrhythmias, and to protect the heart from a second heart attack (myocardial infarction) after a first heart attack (secondary prevention).	Metoprolol, Atenolol, Toprol, Tartrate
Omega 3 (Omeg3)	371 (23.4%)	986 (12.1%)	Polyunsaturated fatty acids with a double bond at the third carbon atom from the end of the carbon chain	Fish, Fatty, Oil, Omega
Multivitamin (multvn)	359 (22.6%)	888 (10.9%)	Preparation intended to be a dietary supplement with vitamins, dietary minerals, and other nutritional elements	Multivitamin, Vitamins, Centrum Silver, Gluconate
Statin (Statn)	346 (21.8%)	844 (10.4%)	Drugs often prescribed by doctors to help lower cholesterol levels in the blood. By lowering the	Simvastatin, Lipitor, Atorvastatin,

			levels, they help prevent heart attacks and stroke.	Pravastatin
Antispastic (Antipc)	340 (21.4%)	1150 (14.2%)	Drug or other agent that suppresses muscle spasms.	Baclofen, Bacoflen, Soma
General sleep (Gene)	322 (020.3%)	767 (9.4%)	Any medication or agent that effects sleep of the patient.	Zolpidem, Provigil, Melatonin, Lunesta
Irreversible cyclooxygenase inhibitor (ici)	319 (20.1%)	774 (9.5%)	Suppress the production of prostaglandins and thromboxanes is due to its irreversible inactivation of the cyclooxygenase (COX) enzyme	Aspirin, Bayer, ASA81, Asprin
Antihistamine (antihe)	313 (19.7%)	735 (9.1%)	Drug that opposes the activity of histamine receptors in the body.	Claritin, Diphenhydramine, Promethazine, Allegra
Proton pump inhibitor (ppi)	290 (18.2%)	700 (8.6%)	Pronounced and long-lasting reduction of gastric acid production.	Omeprazole, Nexium, Pantoprazole, Prilosec
Calcium channel blocker (ccb)	287 (18.1%)	737 (9.1%)	Disrupt the movement of calcium through calcium channels.	Amlodipine, Norvasc, Diltiazem, Verapamil
Acetaminophen (acerin)	282 (17.8%)	631 (7.8%)	Used to treat many conditions such as headache, muscle aches, arthritis, backache, toothaches, colds, and fevers.	Lortab, Acetaminophen, Vicodin, Excedrin
Feeding tube (feedge)	266 (16.8%)	517 (6.4%)	A device that's inserted into your stomach through your abdomen. It's used to supply nutrition when you have trouble eating.	Enteral, Tube, Vivelle, NG
Alternative Herbal Medication (Ahmn)	246 (15.5%)	510 (6.3%)	The study or practice of the medicinal and therapeutic use of plants, now especially as a form of alternative medicine.	Grape, Garlic, Herbal, Ginkgo

Figures

Figure 1: Correlation between the most common disease and intervention categories: Most common was defined as occurring in more than 8.5% of the ALS population. Circular relationship plot: Each 1-pixel line connecting the two categories is where the two categories shared the same patient. Gender is replaced by “male” or “female”, onset type is replaced with “bulbar” or “limb”, onset age is replaced with “>55 years” and “<55 years”, disease duration is replaced with “longer” or “shorter” than average disease duration where the average disease duration is 3.67 years.

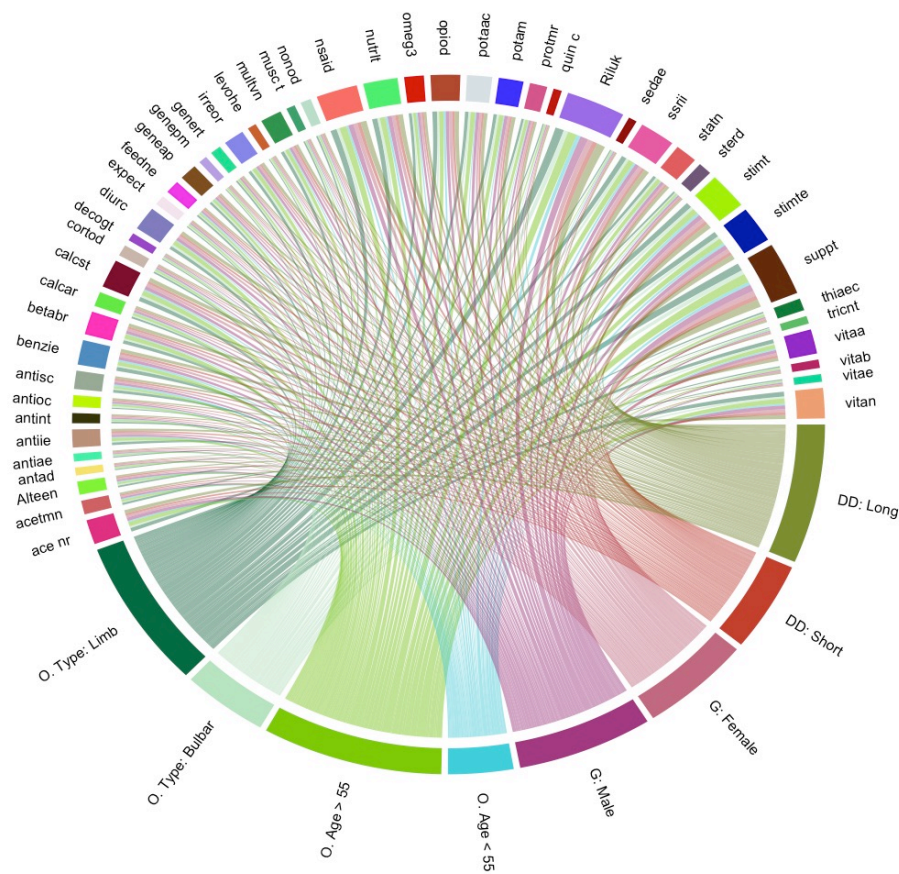


Figure 2: Scree plot for ALS data per patient for disease and intervention categories: Eigenvalue diagram of the factor analysis where the components' eigenvalues do not fall below 1 till the 19th component.

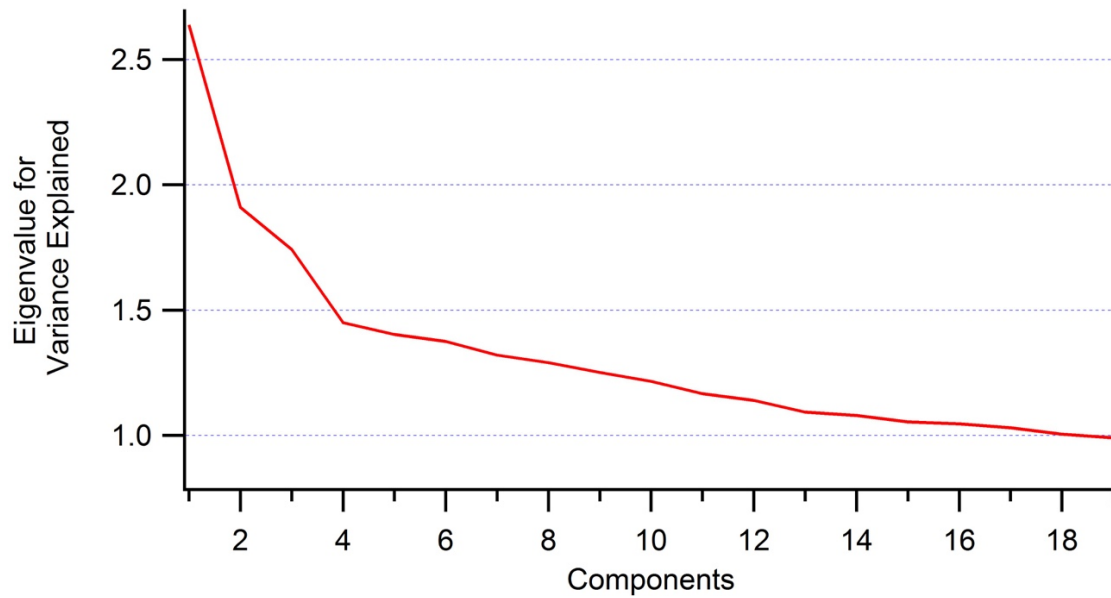


Figure 3: Biplot for the most common categories and the raw data connection to these categories: The vectors were plotted based on the correlation to the two most explanatory eigenvectors created through factor analysis. The closer to one another the more correlated the two vectors are on this mapping, and the more of the same variance they explain.

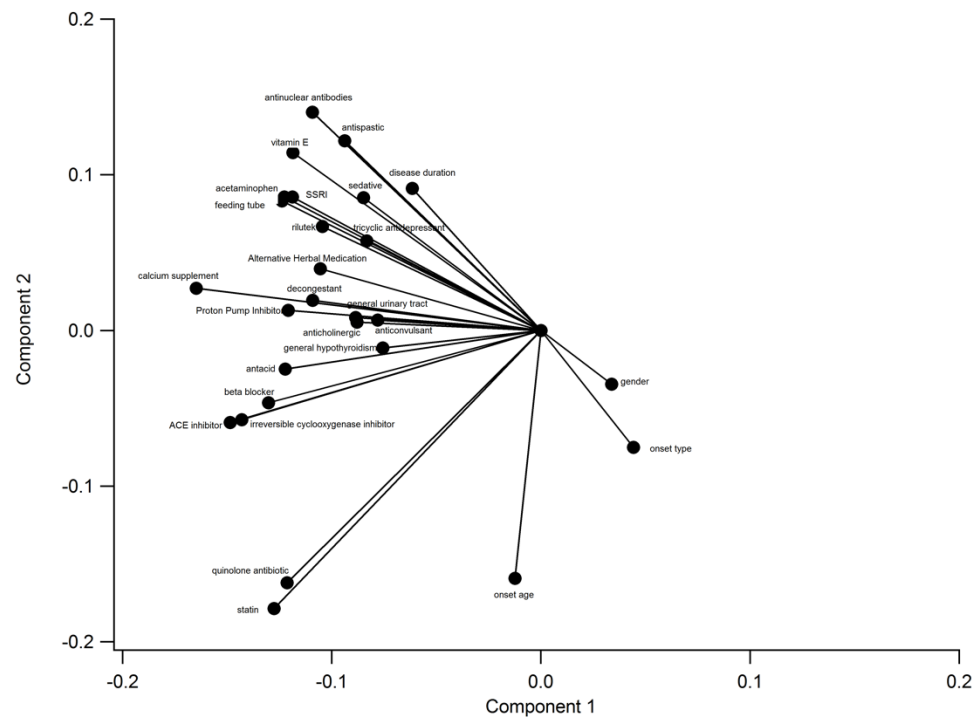


Figure 4: Combination of AUC rankings and significance from the Fisher exact test to show predictability of disease characteristics using the top (8.5%) intervention categories: Random forest determined how much each individual metric contributed to the area under the curve (AUC), and Fisher exact test determined significance. The bars indicate the relative predictive power of the AUC results for predicting each disease characteristic, $p < 0.05$ is marked as “o”, $p < 0.01$ is marked as “*”, $p < 0.001$ is marked as “+”, while “x” marks $p > 0.05$. In all panels, “C” indicates a patient characteristic category as being more predictive than an intervention category; “B” represents a category more predictive of bulbar onset whereas “L” represents a category more predictive of limb onset. “M” represents a category more predictive of male and “F” represents a category more predictive of female. A. Relative importance of categories predicting ALS patient onset type. B. Relative importance of categories predicting ALS patient gender. C. Relative importance of categories predicting ALS patient onset age.

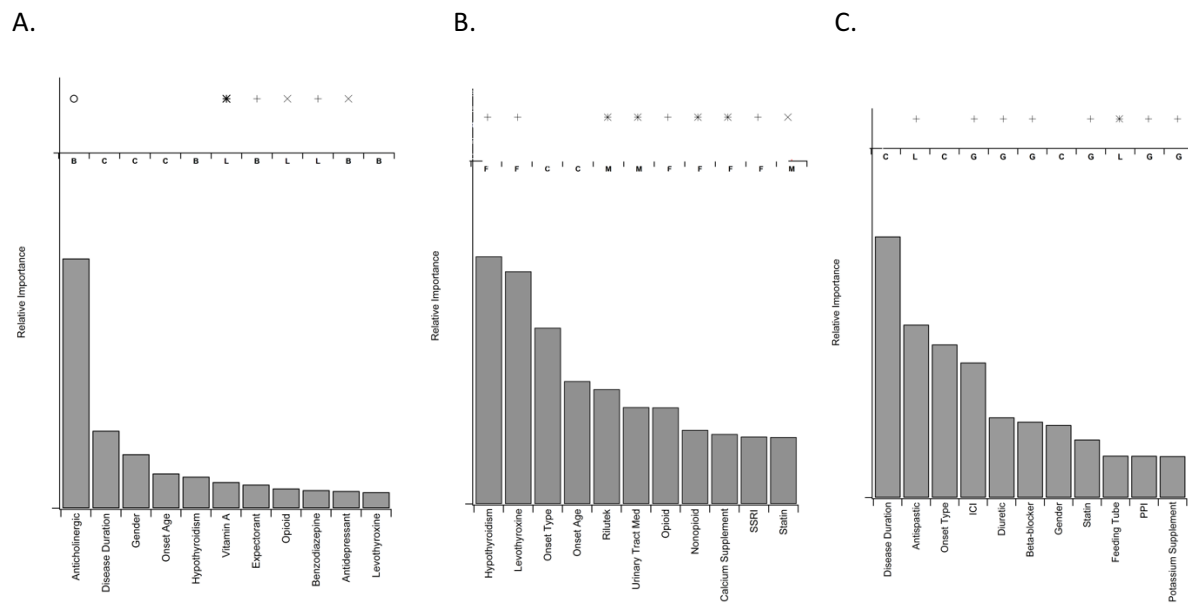


Figure 5: Kaplan-Meier survival analysis to visualize disease duration: Most common (top 8.5%) off-label intervention categories effect on survival. A. Survival for all ALS patients. B. Effect of intervention categories (Rilutek, feeding tube) on survival. C. Effect of varying patient disease characteristics on survival. D. Effect of gender.

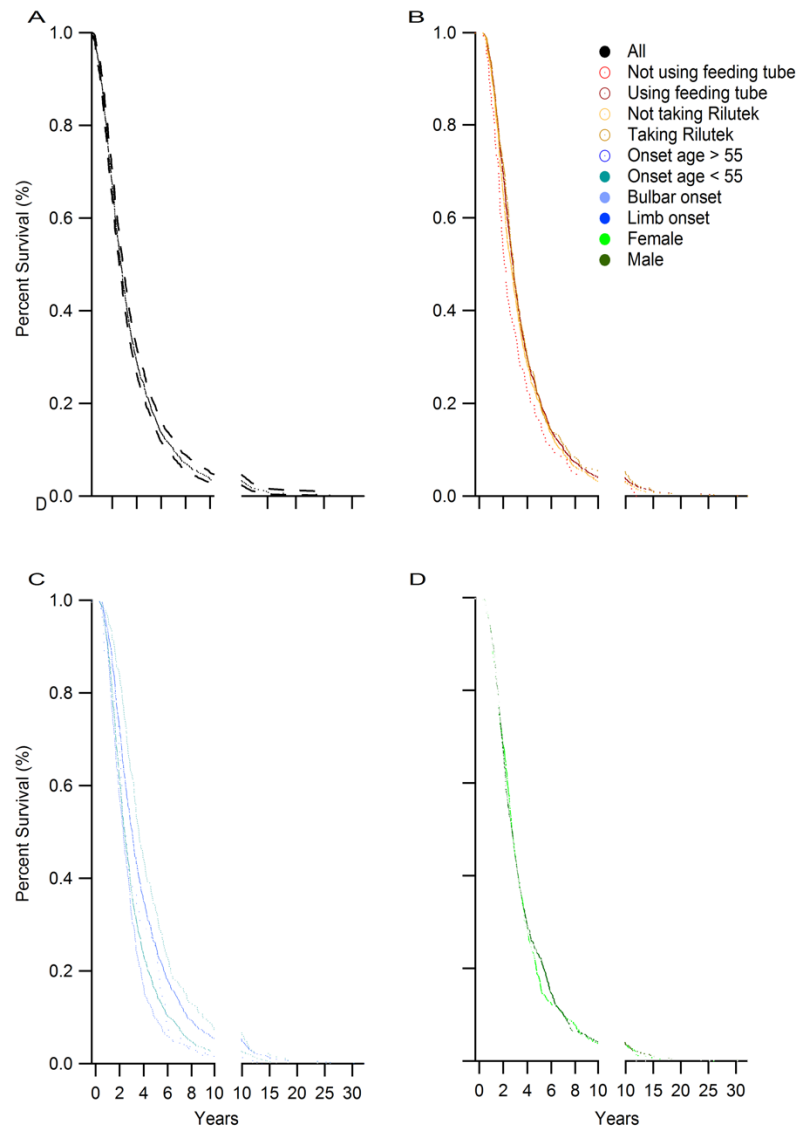
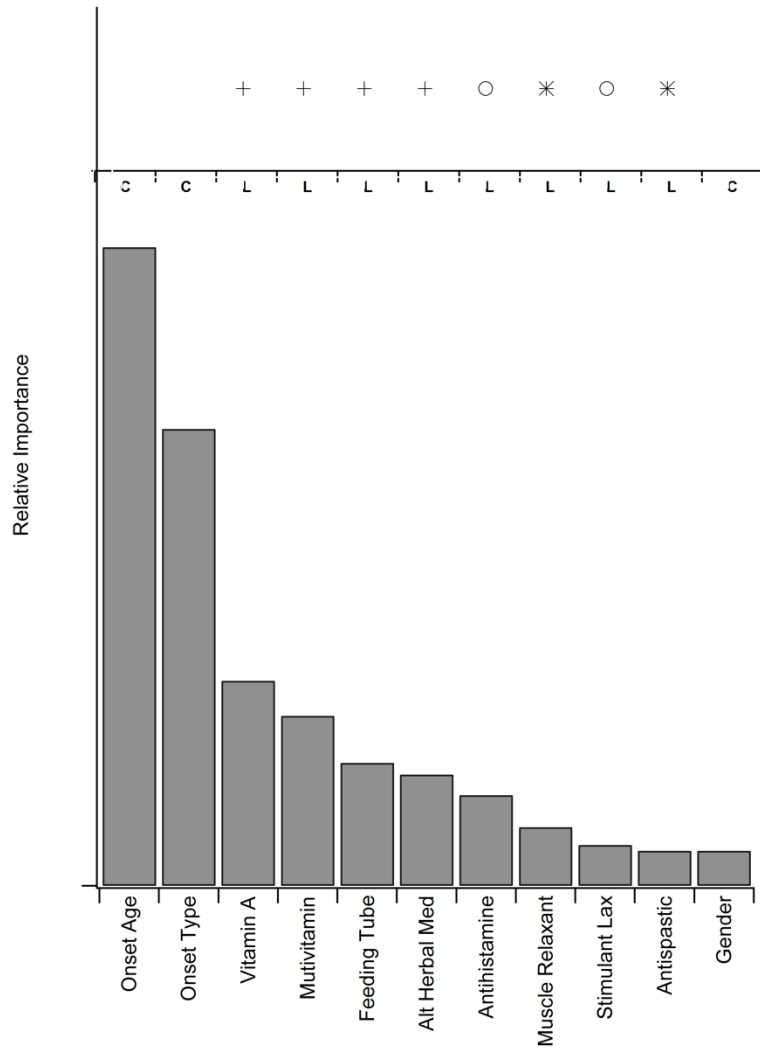


Figure 6: Disease and intervention categories as predictors of ALS disease duration. Random forest was used to determine how much each individual metric helped individually increase the area under the curve (AUC). Fisher exact test was used to determine significance: $p < 0.05$ is marked as “o”, $p < 0.01$ is marked as “*”, and $p < 0.001$ is marked as “+”, and “c” denotes patient characteristic category rather than intervention usage category.



APPENDIX A

Full Table 2 Individual Medications, number of people taking them, number of visits when they were being taken, and intervention categories the medication belongs to.

Medicine	# of visits	# of patients	Intervention. Category
Rilutek	2874	945	ALS treatment
vitamin	658	265	vitamin
baclofen	560	227	antispastic , muscle relaxant
aspirin	357	152	irreversible cyclooxygenase inhibitor , nsaid
multivitamin	234	94	multivitamin
clonazepam	219	89	benzodiazepine
glycopyrrolate	166	80	anticholinergic
lexapro	139	79	ssri
gabapentin	170	77	anticonvulsant , antiepileptic
lisinopril	160	74	ace inhibitor
loratab	131	73	acetaminophen , opioid
fish	141	62	omega 3
calcium	158	59	calcium supplement
cough	104	58	general cough
ambien	96	57	sedative
vitamin e	155	56	vitamin e
topical	134	56	skin ointment
fatty	146	55	omega 3
levothyroxine	131	54	levothyroxine
potassium	114	54	potassium
zoloft	93	52	ssri
tramadol	102	51	analgesic
albuterol	120	49	bronchodilator
xanax	105	49	benzodiazepine
docusate	91	49	stool softener
ibuprofen	133	48	nsaid
coenzyme	95	48	coq10
zolpidem	94	48	general sleep
polyunsaturated	130	47	good fat
metoprolol	96	47	beta blocker
robinul	71	47	general ulcer prevention

quinine	82	45	quinine
hydrochlorothiazide	91	44	potassium-sparing diuretic , thiazide diuretic
paxil	87	44	ssri
prednisone	87	44	corticosteroid
klonopin	63	44	benzodiazepine
tizanidine	96	43	muscle relaxant
citalopram	138	42	ssri
magnesium	92	42	magnesium
lorazepam	74	42	benzodiazepine
omeprazole	77	41	general gastro , proton pump inhibitor
amitriptyline	105	40	tricyclic antidepressant
simvastatin	99	40	statin
alprazolam	92	39	benzodiazepine
synthroid	63	38	levothyroxine
oil	93	37	omega 3
sl	78	36	sublingual
nexium	75	36	proton pump inhibitor
enteral	63	36	feeding tube
trazodone	92	35	trazodone
vitamin c	87	35	vitamin c
amlodipine	82	35	calcium channel blocker
atenolol	77	35	beta blocker
escitalopram	76	35	ssri
sodium	74	34	NA
tylenol	69	34	nonopioid
celebrex	57	34	nsaid
percocet	54	34	opioid
metformin	92	33	lower blood sugar level
vitamin d	75	33	vitamin d
sulfate	60	33	iron
celexa	58	33	ssri
on	46	33	NA
folic	74	30	vitamin b
zanaflex	72	30	muscle relaxant
lipitor	69	30	statin
atorvastatin	64	30	statin
acetaminophen	58	30	acetaminophen

neurontin	44	30	anticonvulsant
vit	39	30	NA
ascorbic	70	29	vitamin c
sertraline	70	29	ssri
chloride	59	28	NA
hyoscyamine	57	28	anticholinergic , antispasmodic
centrum	56	28	multivitamin
inhale	55	28	NA
skilled	47	28	NA
norvasc	41	28	calcium channel blocker
asa	36	28	antacid , nsaid
two	32	27	NA
acids	59	26	NA
tamsulosin	58	26	generl urinary tract
naproxen	51	26	nsaid
qam	48	26	NA
morning	37	26	NA
vitamin b12	61	25	vitamin b
paroxetine	59	25	ssri
fluticasone	57	25	corticosteroid
ophthalmic	53	25	quinolone antibiotic
intl	43	25	NA
peg	43	25	osmotic type laxative
scopolamine	42	25	scopolamine
diazepam	53	24	benzodiazepine
xl	52	24	NA
nuedexta	48	24	stimulant
diovan	47	24	angiotensin ii receptor antagonist
weeks	43	24	NA
hoyer	36	24	patient lift
hydrocodone	26	24	opioid
tacrolimus	78	23	organ donation
colace	53	23	stool softener
potassium chloride	51	23	potassium
toprol	43	23	beta blocker
multiple	41	23	NA
be	33	23	NA
mycophenolate	81	22	immunosuppressant

pravastatin	74	22	statin
mofetil	72	22	immunosuppressant
provigil	46	22	general sleep
atropine	35	22	antimuscarinic
liquid	32	22	NA
senna	29	22	stimulant laxative
enteric	52	21	NA
furosemide	51	21	loop diuretic
effexor	41	21	snri
warfarin	41	21	anticoagulant
transdermal	38	21	NA
complex	37	21	NA
detrol	32	21	general urinary tract
stool	30	21	stool softener
if	27	21	NA
start	25	21	NA
mycophenolate mofetil	65	20	immunosuppressant
creatine	46	20	muscle strengthener
cyanocobalamin	46	20	vitamin b
la(six)	41	20	loop diuretic
lasix	41	20	loop diuretic
flonase	39	20	corticosteroid
pantoprazole	39	20	proton pump inhibitor
speech	38	20	communication
valium	38	20	benzodiazepine
q10	37	20	coq10
cyclobenzaprine	34	20	muscle relaxant
prozac	34	20	ssri
vitamin d3	32	20	vitamin d
elavil	30	20	tricyclic antidepressant
mestinon	28	20	pyridostigmine
ativan	27	20	benzodiazepine
coumadin	27	20	anticoagulant
minerals	46	19	NA
oxycodone	44	19	opioid
prilosec	43	19	proton pump inhibitor
meq	40	19	NA
q8hr	32	19	NA
pt	27	19	support

from	22	19	NA
im	35	18	NA
temazepam	35	18	benzodiazepine
excessive	34	18	NA
film	34	18	NA
vitamin b	32	18	vitamin b
by	31	18	NA
guaifenesin	30	18	expectorant
powder	28	18	skin ointment
ranitidine	28	18	histamine-2 blocker
spray	28	18	NA
zocor	28	18	statin
x	26	18	NA
fentanyl	25	18	opioid
diskus	39	17	corticosteroid , long acting beta agonist
cr	37	17	NA
meloxicam	32	17	nsaid
wellbutrin	32	17	bupropion
Coenzyme Q10	28	17	coq10
bedtime	19	17	NA
hctz	18	17	potassium-sparing diuretic , thiazide diuretic
xr	40	16	NA
folic acid	36	16	vitamin b
advair	35	16	corticosteroid, long acting beta agonist
silver	34	16	NA
pepcid	33	16	histamine-2 blocker
headmaster	28	16	NA
flomax	24	16	generl urinary tract
iv	24	16	nutritional supplement
bipap	22	16	bipap
see	22	16	NA
zetia	22	16	ezetimibe
levsin	20	16	anticholinergic , antispasmodic
morphine	19	16	opioid
advil	46	15	nsaid
ropinirole	43	15	dopamine agonist

seed	42	15	NA
insulin	36	15	insulin
losartan	36	15	angiotensin ii receptor antagonist
docusate sodium	32	15	stool softener
er	32	15	NA
pm	32	15	NA
diltiazem	31	15	calcium channel blocker
prevacid	31	15	proton pump inhibitor
esomeprazole	30	15	proton pump inhibitor
sublingual	30	15	NA
zinc	28	15	zinc supplement
vicodin	26	15	acetaminophen , opioid
la	22	15	NA
allopurinol	21	15	xanthine oxidase inhibitor
claritin	21	15	antihistamine
blood	17	15	NA
baby	16	15	NA
will	15	15	NA
protonix	41	14	proton pump inhibitor
cymbalta	34	14	snri
ds	32	14	NA
outpatient	31	14	support
plavix	30	14	adp receptor inhibitor
fluoxetine	27	14	ssri
premarin	26	14	progesterone
duragesic	25	14	opioid
clopidogrel	24	14	adp receptor inhibitor
oxide	24	14	magnesium
tube	24	14	feeding tube
via	23	14	NA
tartrate	22	14	beta blocker
glycol	20	14	osmotic type laxative
pr	20	14	NA
titrate	18	14	NA
minocycline	17	14	tetracycline antibiotic
nystatin	17	14	nystatin
other	17	14	NA
iron	16	14	iron

carvedilol	36	13	beta blocker
carbonate	34	13	NA
zantac	30	13	histamine-2 blocker
diphenhydramine	29	13	antihistamine
famotidine	27	13	histamine-2 blocker
marinol	27	13	marijuana
zofran	25	13	ondansetron
co	24	13	NA
Centrum Silver	23	13	multivitamin
crestor	21	13	statin
hct	21	13	angiotensin receptor blocker , potassium-sparing diuretic , thiazide diuretic
magnesium oxide	20	13	magnesium
puffs	20	13	NA
drops	18	13	general eye
hrs	17	13	NA
miralax	17	13	osmotic type laxative
flexeril	16	13	muscle relaxant
no	16	13	NA
half	15	13	NA
promethazine	15	13	antihistamine , general nausea , general vomiting
not	14	13	NA
pain	14	13	NA
omega	28	12	omega 3
diclofenac	26	12	nsaid
glucosamine	26	12	glucosamine
seroquel	26	12	atypical antipsychotic
vitamins	22	12	multivitamin
doxazosin	21	12	generl urinary tract
hospital	21	12	support
allegra	20	12	antihistamine
benicar	19	12	angiotensin receptor blocker
polyethylene	18	12	bulk forming laxative
polyethylene glycol	18	12	bulk forming laxative
hs	17	12	NA
rt	17	12	NA
night	15	12	NA

over	13	12	NA
mvi	12	12	multivitamin
terazosin	32	11	general urinary tract
melatonin	30	11	general sleep
bupropion	27	11	bupropion
oxycontin	27	11	opioid
nitroglycerin	26	11	nitrate
toe	25	11	NA
glimepiride	22	11	insulin
glipizide	22	11	insulin
benadryl	21	11	antihistamine
hr	21	11	NA
toprol xl	20	11	beta blocker
mucinex	19	11	cough suppressant , expectorant
zyrtec	19	11	antihistamine
cream	17	11	skin ointment
saw	17	11	NA
liver	16	11	general gastro
metoclopramide	16	11	metoclopramide
pill	15	11	NA
bisacodyl	12	11	stimulant laxative
ferrous	34	10	iron
aerosol	32	10	NA
rosuvastatin	28	10	statin
digoxin	24	10	cardiac glycoside
taken	22	10	NA
cozaar	21	10	angiotensin receptor blocker
nortriptyline	21	10	tricyclic antidepressant
app	20	10	NA
milk	20	10	NA
aleve	18	10	general antiplatelet
beta	18	10	NA
ipratropium	18	10	bronchodilator
misc	18	10	NA
lipoic	17	10	antioxidant
modafinil	17	10	awakefulness
viagra	17	10	phosphodiesterase inhibitor
plus	16	10	NA

reglan	16	10	metoclopramide
ondansetron	15	10	ondansetron
lunesta	14	10	general sleep
robitussin	14	10	cough suppressant , decongestant , expectorant
noon	12	10	NA
but	11	10	NA
may	11	10	NA
pills	11	10	NA
trial	11	10	NA
motrin	10	10	nsaid
titrated	10	10	NA
succinate	30	9	beta blocker
loratadine	28	9	antihistamine
quinidine	26	9	anti arrhythmic
cfc	22	9	NA
nasonex	22	9	corticosteroid
hfa	21	9	bronchodilator
physical	21	9	support
combivent	20	9	bronchodilator
right	19	9	NA
st	18	9	NA
eye	17	9	general eye
pravachol	17	9	statin
therapy	17	9	NA
gel	16	9	skin ointment
venlafaxine	15	9	snri
lidoderm	14	9	anesthetic
namenda	14	9	n-methyl-d-aspartate-receptor antagonist
next	14	9	NA
table	14	9	NA
left	13	9	NA
verapamil	13	9	calcium channel blocker
cellcept	12	9	immunosuppressant
dulcolax	12	9	stimulant laxative
mirtazapine	12	9	mirtazapine
rectal	12	9	rectal test
taking	12	9	NA

tolterodine	12	9	generl urinary tract
levaquin	11	9	fluoroquinolone
pressure	10	9	NA
subcutan	10	9	NA
titrating	10	9	NA
sinemet	28	8	carbidopa , levodopa
grape	23	8	Alternative Herbal Medication
garlic	21	8	Alternative Herbal Medication
mirapex	20	8	dopamine agonist
Mirapex	20	8	dopamine agonist
singular	20	8	leukotriene inhibitor
probiotic	19	8	general antibiotic
cholecalciferol	18	8	vitamin d
multiple vitamins	17	8	multivitamin
symbicort	17	8	corticosteroid , long acting beta agonist
sprays	16	8	NA
alpha	15	8	NA
regular	15	8	NA
substitution	15	8	NA
trileptal	15	8	antiepileptic
mometasone	14	8	topical steroid
multivitamins	14	8	multivitamin
bactrim	13	8	sulfamethoxazole , trimethoprim
electrolyte	13	8	NA
hand	13	8	NA
megestrol	13	8	progesterone
ergocalciferol	12	8	vitamin d
m	12	8	NA
portable	12	8	NA
bacoflen	11	8	antispastic , muscle relaxant
suspension	11	8	NA
ophthalmic	10	8	quinolone antibiotic
enoxaparin	9	8	anticoagulant
ultram	9	8	opioid
clonidine	25	7	thiazide diuretic
cetirizine	23	7	antihistamine
valganciclovir	23	7	cmv antiviral , organ transplant

testosterone	21	7	testosterone
aspir	19	7	irreversible cyclooxygenase inhibitor , nsaid
finasteride	19	7	generl urinary tract
oxybutynin	18	7	generl urinary tract
strength	16	7	muscle strengthener
levoxyl	15	7	levothyroxine
study	14	7	NA
allergy	13	7	general allergie
caltrate	13	7	calcium supplement
lactulose	13	7	colonic acidifier
lotrel	13	7	ace inhibitor
tsp	13	7	NA
benazepril	12	7	ace inhibitor
can	12	7	nutritional supplement
fosamax	12	7	antiresorptive
hydralazine	12	7	vasodilator
lantus	12	7	insulin glargine
first	11	7	NA
low	11	7	NA
spironolactone	11	7	potassium-sparing diuretic
triamcinolone	11	7	anti inflammatory , antipruritic agent
valsartan	11	7	angiotensin ii receptor antagonist
cans	10	7	nutritional supplement
fluconazole	10	7	azole antifungal
kcl	10	7	potassium
nutrition	10	7	nutritional supplement
restoril	10	7	benzodiazepine
ubiquinone	10	7	coq10
alendronate	9	7	antiresorptive
trazadone	9	7	trazedone
water	9	7	water
darvocet	8	7	opioid
naprosyn	8	7	nsaid
otc	8	7	NA
phenergan	8	7	antihistamine , general nausea , general vomiting , sedative , promethazine

softener	8	7	stool softener
takes	8	7	NA
ultra	8	7	NA
anxiety	7	7	general anxiety
due	7	7	NA
new	7	7	NA
six	7	7	NA
which	7	7	NA
chondroitin	20	6	chondroitin
enalapril	19	6	ace inhibitor
dextromethorphan	17	6	cough suppressant
into	17	6	NA
pramipexole	16	6	dopamine agonist
barium	15	6	contrast agent
coreg	15	6	beta blocker
excedrin	15	6	acetaminophen , stimulant , nsaid
extract	15	6	NA
modified	15	6	NA
voltaren	15	6	nsaid
elevated	13	6	NA
mouth	13	6	NA
proair	13	6	bronchodilator
estradiol	12	6	estrogen
fenofibrate	12	6	fibrate
imitrex	12	6	selective serotonin receptor agonists, nsaid
isosorbide	12	6	nitrate
off	12	6	NA
ophthalmic (solution)	12	6	quinolone antibiotic
Wellbutrin XL	12	6	bupropion
both	11	6	NA
minutes	11	6	NA
ot	11	6	support
pump	11	6	NA
rollator	11	6	skeletal support
thyroid	11	6	general hypothyroidism
ventolin	11	6	bronchodilator
custom	10	6	NA

donepezil	10	6	donepezil
glucophage	10	6	insulin
doxycycline	9	6	tetracycline antibiotic
lovenox	9	6	enoxaparin sodium
meclizine	9	6	antihistamine
muscle	9	6	NA
until	9	6	NA
avapro	8	6	angiotensin ii receptor blocker
ezetimibe	8	6	ezetimibe
lansoprazole	8	6	proton pump inhibitor
meals	8	6	nutritional supplement
occupational	8	6	support
requip	8	6	ropinirole
actos	7	6	glitazone
citrate	7	6	NA
riluzole (in other medications)	7	6	als treatment
side	7	6	NA
spiriva	7	6	bronchodilator
suction	7	6	suction machine
teaspoons	7	6	NA
bed	6	6	NA
cod	6	6	NA
hcl	6	6	NA
high	6	6	marijuana?
is	6	6	NA
started	6	6	NA
fexofenadine	15	5	antihistamine
wheeled	15	5	skeletal support
flax	14	5	fiber , omega 3
Grape seed extract	14	5	Alternative Herbal Medication
niacin	14	5	niacin , vitamin b
triamterene	14	5	potassium sparing diuretic , thiazide diuretic
lopressor	13	5	beta blocker
pioglitazone	13	5	thiazolidinedione
depakote	12	5	anticonvulsant , antiepileptic
latanoprost	12	5	prostaglandin analog
toilet	12	5	skeletal support
ditropan	11	5	generl urinary tract

memantine	11	5	n-methyl-d-aspartate-receptor antagonist
tnf	11	5	tumour necrosi factor
conjugated	10	5	monoclonal antibodie
extra	10	5	NA
formula	10	5	NA
quetiapine	10	5	atypical antipsychotic
atrovent	9	5	bronchodilator
benztropine	9	5	dopamine agonist
divalproex	9	5	anticonvulsant , antiepileptic
migraine	9	5	general head pain
qpm	9	5	NA
roxicet	9	5	opioid
sotalol	9	5	beta blocker
topamax	9	5	antiepileptic
u	9	5	NA
vytorin	9	5	statin
dm	8	5	cough suppressant , expectorant
food	8	5	nutritional supplement
go	8	5	NA
jevity	8	5	nutritional supplement
manual	8	5	NA
metamucil	8	5	bulk forming laxative
resting	8	5	general sleep
sterile	8	5	NA
stop	8	5	NA
adderall	7	5	stimulant
aricept	7	5	donepezil
respiratory	7	5	general breathing
total	7	5	NA
valtrex	7	5	herpe antiviral
benzonatate	6	5	tessalon perle
ivpb	6	5	NA
levothroid	6	5	levothyroxine
odt	6	5	NA
power	6	5	NA
vesicare	6	5	urinary muscle spasm
vitamin a	6	5	vitamin a

accupril	5	5	ace inhibitor
amino	5	5	NA
bolus	5	5	NA
clotrimazole	5	5	azole antifungal
diflucan	5	5	azole antifungal
excess	5	5	NA
herbal	5	5	Alternative Herbal Medication
human	5	5	NA
labetalol	5	5	beta blocker
methylphenidate	5	5	stimulant
month	5	5	NA
pamelor	5	5	tricyclic antidepressant
reconstitution	5	5	NA
rilutek (in other medications)	5	5	als treatment
shoulder	5	5	NA
sinus	5	5	general sinus , general breathing
some	5	5	NA
vioxx	5	5	nsaid
weekly	5	5	NA
ramipril	18	4	ace inhibitor
biotin	15	4	vitamin b
estrace	13	4	estrogen
ferrous sulfate	13	4	iron
imodium	13	4	loperamide
cipro	12	4	fluoroquinolone
drop	12	4	general eye
fosinopril	12	4	ace inhibitor
sildenafil	12	4	phosphodiesterase inhibitor
ginkgo	11	4	Alternative Herbal Medication
actonel	10	4	antiresorptive
azelastine	10	4	antihistamine
cialis	10	4	tadalafil
montelukast	10	4	leukotriene receptor antagonist
osteo	10	4	general bone
swallow	10	4	general excess saliva
avodart	9	4	dutasteride
dronabinol	9	4	marijuana
maxzide	9	4	potassium-sparing diuretic ,

			thiazide diuretic
puff	9	4	NA
robaxin	9	4	muscle relaxant
super	9	4	NA
amaryl	8	4	sulfonylurea
bystolic	8	4	beta blocker
contin	8	4	opioid
coq	8	4	coq10
gluconate	8	4	multivitamin
levalbuterol	8	4	bronchodilator
lift	8	4	patient lift
lovastatin	8	4	statin
ms	8	4	vision loss, pain, fatigue, and impaired coordination
niaspan	8	4	vitamin b
prostate	8	4	rectal test
q6hrs	8	4	NA
simethicone	8	4	simethicone
xarelto	8	4	anticoagulant
xopenex	8	4	brochospasm
bedside	7	4	NA
citrucel	7	4	bulk forming laxative
flagyl	7	4	nitroimidazole
laxative	7	4	general constipation
lidocaine	7	4	anesthetic
prinivil	7	4	ace inhibitor
q72hr	7	4	NA
aciphex	6	4	proton pump inhibitor
buspirone	6	4	bupropion
klor-con	6	4	potassium
levofloxacin	6	4	quinolone antibiotic
lithium	6	4	antimanic
methadone	6	4	opioid
methylprednisolone	6	4	corticosteroid
palmetto	6	4	Alternative Herbal Medication
q6h	6	4	NA
q72	6	4	NA
subcutaneous	6	4	NA
timolol	6	4	beta blocker

tiotropium	6	4	anticholinergic
afo	5	4	NA
carnitine	5	4	amino acid
celecoxib	5	4	nsaid
evista	5	4	selective estrogen receptor modulator
gemfibrozil	5	4	fibrate
glycopyrolate	5	4	anticholinergic
international	5	4	NA
keflex	5	4	cephalosporin antibiotic
maximum	5	4	NA
mobic	5	4	nsaid
morphine sulfate	5	4	opioid
q5min	5	4	NA
remeron	5	4	mirtazapine
soln	5	4	NA
supp	5	4	NA
syrup	5	4	NA
trach	5	4	tracheostomy tube
unknown	5	4	NA
vit E	5	4	vitamin e
amoxicillin	4	4	penicillin
an	4	4	NA
back	4	4	NA
bayer	4	4	irreversible cyclooxygenase inhibitor , nsaid
benedryl	4	4	antihistamine
counter	4	4	NA
during	4	4	NA
ea	4	4	NA
five	4	4	NA
has	4	4	NA
head	4	4	NA
leg	4	4	NA
mineral	4	4	NA
n	4	4	NA
nighttime	4	4	NA
orla	4	4	NA
robinol	4	4	general ulcer prevention

senokot	4	4	stimulant laxative
several	4	4	NA
she	4	4	NA
starting	4	4	NA
steroid	4	4	steroid
through	4	4	NA
was	4	4	NA
coconut	14	3	nutritional supplement
Coenzyme-Q	12	3	coq10
dantrolene	12	3	muscle relaxant
dexilant	12	3	proton pump inhibitor
msm	12	3	methylsulfonylmethane
methotrexate	11	3	antimetabolite
unisom	11	3	antihistamine , doxylamine
valacyclovir	11	3	herpe antiviral
alfuzosin	10	3	generl urinary tract
buffered	10	3	NA
ecotrin	10	3	nsaid
hydrocortisone	10	3	hydrocortisone
metronidazole	10	3	metronidazole
rhinocort	10	3	budesonide , corticosteroid
ginseng	9	3	Alternative Herbal Medication
levetiracetam	9	3	anticonvulsant
theophylline	9	3	xanthine
astepro	8	3	antihistamine
carotene	8	3	vitamin a
dilaudid	8	3	opioid
eszopiclone	8	3	general sleep
macrobid	8	3	nitrofurantoin
mononitrate	8	3	nitrate
vivelle	8	3	feeding tube
cinnamon	7	3	nutritional supplement
clarinex	7	3	antihistamine
magnesia	7	3	magnesium
milk of magnesia	7	3	osmotic type laxative
naltrexone	7	3	opiate antagonist
nitrate	7	3	nitrate
pristiq	7	3	snri
solifenacin	7	3	urinary muscle spasm

vaginal	7	3	NA
botox	6	3	botulinum toxin
clinic	6	3	NA
condom	6	3	contraceptive
coq10	6	3	coq10
dexamethasone	6	3	steroid
eyes	6	3	general eye
full	6	3	NA
novolin	6	3	insulin
q6	6	3	NA
quinapril	6	3	ace inhibitor
red	6	3	NA
rice	6	3	NA
vasotec	6	3	ace inhibitor
yeast	6	3	yeast infection treatment
acidophilus	5	3	lactobacillu
amiodipine	5	3	calcium channel blocker
etodolac	5	3	nsaid
fiber	5	3	nutritional supplement
irrigation	5	3	NA
janumet	5	3	lower blood sugar level
lyrica	5	3	nonopioid
ordered	5	3	NA
propranolol	5	3	beta blocker
seven	5	3	NA
tums	5	3	antacid
Ventolin HFA	5	3	bronchodilator
vitamin d2	5	3	vitamin d
xt	5	3	calcium channel blocker
ab	4	3	NA
acetylcysteine	4	3	acetylcysteine
all	4	3	NA
altace	4	3	ace inhibitor
armodafinil	4	3	stimulant
armour	4	3	thyroid medication
bilateral	4	3	NA
cell	4	3	NA
ciprofloxacin	4	3	fluoroquinolone
clindamycin	4	3	clindamycin

decrease	4	3	NA
dilantin	4	3	anticonvulsant , antiepileptic
ginko	4	3	Alternative Herbal Medication
hydroxyzine	4	3	antihistamine
ibuprofin	4	3	nsaid
klonipin	4	3	benzodiazepine
levothyroid	4	3	levothyroxine
longer	4	3	NA
megace	4	3	progesterone
membrane	4	3	NA
mucous	4	3	expectorant
neb	4	3	NA
norco	4	3	acetaminophen , opioid
pack	4	3	NA
prograf	4	3	organ donation
proscar	4	3	generl urinary tract
qmonth	4	3	NA
relief	4	3	NA
ritalin	4	3	stimulant
scheduled	4	3	NA
seating	4	3	NA
selenium	4	3	antioxidant
sumatriptan	4	3	selective serotonin receptor agonists, nsaid
trikor	4	3	fibrate
unites	4	3	NA
zestoretic	4	3	ace inhibitor , potassium-sparing diuretic
azithromycin	3	3	macrolide type antibiotic
call	3	3	NA
catheter	3	3	generl urinary tract
chest	3	3	general heart
dantrium	3	3	muscle relaxant
delsym	3	3	cough suppressant
enzyme	3	3	NA
fax	3	3	NA
felodipine	3	3	calcium channel blocker
flaxseed	3	3	fiber , omega 3
foot	3	3	NA

gas	3	3	NA
glutathione	3	3	Alternative Herbal Medication
growth	3	3	NA
hydromorphone	3	3	opioid
ivig	3	3	immunoglobulin
lfts	3	3	liver test
master	3	3	NA
md	3	3	NA
meperidine	3	3	opioid
micrograms	3	3	NA
multi	3	3	NA
nebulizer	3	3	NA
necessary	3	3	NA
neudexta	3	3	stimulant
ng	3	3	feeding tube
nifedipine	3	3	calcium channel blocker
nudexta	3	3	stimulant
nutritional	3	3	nutritional supplement
ointment	3	3	skin ointment
only	3	3	NA
oxcarbazepine	3	3	anticonvulsant
past	3	3	NA
pls	3	3	NA
prescription	3	3	NA
previously	3	3	NA
primrose	3	3	omega 3
prochlorperazine	3	3	antipsychotic
pyridostigmine	3	3	pyridostigmine
q4hrs	3	3	NA
quaifenesin	3	3	expectorant
s	3	3	NA
shortness	3	3	NA
shots	3	3	NA
since	3	3	NA
sleep	3	3	general sleep
sliding	3	3	NA
soma	3	3	antispastic , muscle relaxant
sr	3	3	NA
sudafed	3	3	pseudoephedrine

tablespoon	3	3	NA
today	3	3	NA
treatment	3	3	NA
try	3	3	NA
ursodiol	3	3	ursodiol
used	3	3	NA
when	3	3	NA
intrathecal	13	2	drug helper
carafate	12	2	general ulcer prevention
psyllium	11	2	bulk forming laxative
nuvigil	10	2	general sleep
darifenacin	9	2	general urinary tract
grapeseed	9	2	Alternative Herbal Medication
prazosin	9	2	alpha adrenergic blocker
betamethasone	8	2	nonopioid
bicalutamide	8	2	anti androgen
biloba	8	2	Alternative Herbal Medication
buspar	8	2	bupropion
dipropionate	8	2	corticosteroid
zithromax	8	2	azithromycin
es	7	2	NA
guanfacine	7	2	guanfacine
januvia	7	2	lower blood sugar level
lotion	7	2	skin ointment
soft	7	2	NA
vitamin b1	7	2	vitamin b
codeine	6	2	opioid
copper	6	2	copper
dark	6	2	NA
esterified	6	2	estrogen , methyltestosterone
glyburide	6	2	insulin
metanx	6	2	Alternative Herbal Medication
nicotine	6	2	general sleep
p	6	2	NA
sulindac	6	2	nsaid
augmentin	5	2	penicillin
brimonidine	5	2	alpha agonist
cardizem	5	2	calcium channel blocker
dextomethorphan	5	2	cough suppressant

elbow	5	2	NA
elemental	5	2	NA
fluocinonide	5	2	steroid
hyzaar	5	2	angiotensin receptor blocker
iosartan	5	2	angiotensin ii receptor antagonist
late	5	2	NA
levitra	5	2	vardeafil
methocarbamol	5	2	muscle relaxant
perocet	5	2	acetaminophen , opioid
phosphate	5	2	phosphate inhibitor
solostar	5	2	insulin
tadalafil	5	2	tadalafil
telmisartan	5	2	angiotensin ii receptor antagonist
tongue	5	2	NA
topiramate	5	2	antiepileptic
under	5	2	NA
vardeafil	5	2	phosphodiesterase inhibitor , vardeafil
withhold	5	2	NA
work	5	2	purpose
alphagan	4	2	alpha agonist
amantadine	4	2	influenza a antiviral
amiodarone	4	2	anti arrhythmic
amitryptiline	4	2	tricyclic antidepressant
asa81	4	2	irreversible cyclooxygenase inhibitor , nsaid
atorvastin	4	2	statin
bextra	4	2	nsaid
coasted	4	2	ovarian hyperstimulation
colchicine	4	2	colchicine
directed	4	2	NA
epa	4	2	omega 3
famciclovir	4	2	herpe antiviral
green	4	2	marijuana?
hydroxyurea	4	2	cancer treatment
i	4	2	NA
ketotifen	4	2	antihistamine
ocuvite	4	2	multivitamin

ofetil	4	2	immunosuppressant
provera	4	2	progestin
pulmicort	4	2	corticosteroid
selenious	4	2	selenium
setraline	4	2	ssri
shower	4	2	support
taztia	4	2	aminosalicylate
use	4	2	NA
abilify	3	2	atypical antipsychotic
adalat	3	2	calcium channel blocker
adapter	3	2	NA
allard	3	2	NA
ambian	3	2	sedative
antioxidant	3	2	antioxidant
bimatoprost	3	2	prostaglandin analog
citracal	3	2	calcium supplement
cmp	3	2	test
cranberry	3	2	generl urinary tract
dhea	3	2	testosterone
driving	3	2	NA
duloxetine	3	2	snri
epidural	3	2	calcium channel blocker
ester	3	2	NA
estratest	3	2	estrogen , methyltestosterone
exceed	3	2	NA
exelon	3	2	dopamine agonist
flecainide	3	2	anti arrhythmic
fleet	3	2	stimulant laxative
forte	3	2	muscle relaxant
gem	3	2	NA
hydrochloride	3	2	NA
ibuprofen	3	2	nsaid
ir	3	2	support
johns	3	2	NA
klor	3	2	potassium
less	3	2	NA
loaner	3	2	NA
long	3	2	NA
loperamide	3	2	antidiarrheal

lotensin	3	2	ace inhibitor
lumigan	3	2	lumigan ophthalmic
midday	3	2	NA
mis	3	2	NA
neck	3	2	NA
olmesartan	3	2	angiotensin ii receptor antagonist
ou	3	2	NA
pindolol	3	2	beta blocker
polyunsaturated	3	2	NA
pregabalin	3	2	nonopioid
prior	3	2	NA
proventil	3	2	bronchodilator
pseudoephedrine	3	2	decongestant
q1	3	2	NA
reduce	3	2	NA
removal	3	2	NA
salivation	3	2	general excess saliva
social	3	2	communication
syringe	3	2	NA
t	3	2	NA
tears	3	2	NA
vitamin	3	2	NA
vyvanse	3	2	stimulant
zelnorm	3	2	tegaserod
acetaminophen	2	2	acetaminophen
activan	2	2	benzodiazepine
afos	2	2	NA
afrin	2	2	decongestant
als	2	2	NA
androgel	2	2	testosterone
antibiotics	2	2	general antibiotic
any	2	2	NA
ap	2	2	NA
apap	2	2	acetaminophen
arava	2	2	nsaid
ascorbic	2	2	vitamin c
aspirin	2	2	irreversible cyclooxygenase inhibitor , nsaid

asthma	2	2	general asthma
baclofen	2	2	antispastic , muscle relaxant
balcofen	2	2	antispastic , muscle relaxant
bisoprolol	2	2	beta blocker
bp	2	2	blood pressure
carisoprodol	2	2	muscle relaxant
cephalexin	2	2	cephalosporin antibiotic
chain	2	2	NA
chair	2	2	NA
chew	2	2	NA
chinese	2	2	NA
clonazep	2	2	benzodiazepine
clonopin	2	2	benzodiazepine
compression	2	2	NA
cortisol	2	2	cortisol
cosamin	2	2	chondroitin , glucosamine
couple	2	2	NA
creatinine	2	2	muscle strengthener
cretin	2	2	muscle strengthener
cyclbenzaprine	2	2	muscle relaxant
cytoxan	2	2	chemotherapy
depression	2	2	general antidepressant
desyrel	2	2	desyrel
detemir	2	2	insulin detemir
diagnosis	2	2	NA
did	2	2	NA
dinner	2	2	nutritional supplement
disintegrating	2	2	NA
double	2	2	NA
drainage	2	2	NA
dyazide	2	2	potassium-sparing diuretic , thiazide diuretic
ensure	2	2	muscle strengthener
enzymes	2	2	NA
epap	2	2	epap
estrogen	2	2	estrogen
fioricet	2	2	acetaminophen
flecainide	2	2	anti arrhythmic
folate	2	2	vitamin b

further	2	2	NA
gabaprotein	2	2	anticonvulsant , antiepileptic
gabitril	2	2	anticonvulsant , antiepileptic
gabpentin	2	2	anticonvulsant , antiepileptic
geritol	2	2	multivitamin
gingko	2	2	Alternative Herbal Medication
glycolax	2	2	osmotic type laxative
goal	2	2	NA
gradually	2	2	NA
h2o	2	2	water
had	2	2	NA
have	2	2	NA
having	2	2	NA
hc	2	2	NA
headache	2	2	general head pain
heparin	2	2	anticoagulant
him	2	2	NA
hip	2	2	NA
holly	2	2	NA
hormone	2	2	general hormone
hyoscyamin	2	2	anticholinergic , antispasmodic
id	2	2	NA
including	2	2	NA
inhaled	2	2	NA
inhaler	2	2	NA
intramuscular	2	2	NA
intravenous	2	2	NA
it	2	2	NA
klorcon	2	2	potassium
konopin	2	2	benzodiazepine
lactobacillus	2	2	general gastro
lamisil	2	2	terbinafine hydrochloride
levsinex	2	2	anticholinergic , antispasmodic
life	2	2	NA
lispro	2	2	insulin
live	2	2	NA
lodine	2	2	nsaid
lorcet	2	2	opioid
lowering	2	2	NA

lunch	2	2	nutritional supplement
made	2	2	NA
mag	2	2	magnesium
max	2	2	NA
mdi	2	2	NA
meds	2	2	NA
mega	2	2	NA
metprolol	2	2	beta blocker
metoprolol	2	2	beta blocker
micardis	2	2	angiotensin ii receptor antagonist
mid	2	2	NA
min	2	2	NA
miraplex	2	2	dopamine agonist
months	2	2	NA
mornings	2	2	NA
moth	2	2	NA
mynocycline	2	2	tetracycline antibiotic
nasacort	2	2	triamcinolone acetonide
nature	2	2	NA
nausea	2	2	general nausea
nightly	2	2	NA
novolog	2	2	insulin
ns	2	2	nutritional supplement
nsaids	2	2	nsaid
nursing	2	2	support
occasionally	2	2	NA
olpidem	2	2	hypnotic
overheard	2	2	NA
oxytrol	2	2	oxybutynin
pantaprazole	2	2	proton pump inhibitor
paraфон	2	2	muscle relaxant
perles	2	2	tessalon perle
peroxide	2	2	antiseptic
phenobarbital	2	2	barbiturate
phone	2	2	NA
please	2	2	NA
pn	2	2	NA
possible	2	2	NA

prempo	2	2	estrogen , progesterone
prescribed	2	2	NA
primidone	2	2	anticonvulsant
pro	2	2	NA
prune	2	2	general ib
pseudobulbar	2	2	ssri
pyridoxine	2	2	vitamin b
q10min	2	2	coq10
q2hr	2	2	NA
q4h	2	2	NA
q8h	2	2	NA
recommend	2	2	NA
referral	2	2	NA
risperdal	2	2	antipsychotic
rn	2	2	NA
rubinol	2	2	glycopyrrolate_
saline	2	2	NA
saliva	2	2	general exces saliva
saltropine	2	2	general exces saliva
sertaline	2	2	ssri
shot	2	2	NA
sim	2	2	NA
skelaxin	2	2	blocking nerve impulse
slow	2	2	NA
so	2	2	NA
softgel	2	2	NA
sorbitol	2	2	osmotic type laxative
stair	2	2	NA
stopped	2	2	NA
suggested	2	2	NA
supplement	2	2	NA
suppositories	2	2	NA
sure	2	2	NA
tablespoons	2	2	NA
tamazepam	2	2	general sleep
tapering	2	2	NA
teaspoon	2	2	NA
tessalon	2	2	tessalon perle
test	2	2	NA

tetracycline	2	2	tetracycline antibiotic
therapeutic	2	2	NA
thereafter	2	2	NA
thiamine	2	2	vitamin b
tilogy	2	2	plcae?
tip	2	2	NA
tobramycin	2	2	aminoglycoside antibiotic
torse mide	2	2	loop diuretic
transfer	2	2	NA
tranxene	2	2	benzodiazepine
tried	2	2	NA
troche	2	2	azole antifungal
tropical	2	2	skin ointment
unit	2	2	NA
using	2	2	NA
uti	2	2	urinary tract infection antibiotic
vanquish	2	2	nonopioid
vastatin	2	2	statin
vitmain	2	2	NA
wean	2	2	support
wheat	2	2	nutritional supplement
x1	2	2	NA
xp	2	2	NA
zestril	2	2	ace inhibitor
fiorinal	13	1	analgesic , nsaid , sedative , stimulant
digitek	8	1	cardiac glycoside
gtube	8	1	feeding tube
cefdinir	7	1	cephalosporin antibiotic
lamictal	7	1	anticonvulsant , antiepileptic
methysulfonylmethane	7	1	methysulfonylmethane
trusopt	7	1	carbonic anhydrase inhibitor
acyclovir	6	1	herpe antiviral
bulking	6	1	bulking agent
clorazepate	6	1	benzodiazepine
ethopropazine	6	1	dopamine agonist
roxicodone	6	1	opioid
rozerem	6	1	sedative
aakg	5	1	alpha-ketoglutarate

acetyl	5	1	antioxidant
bi	5	1	NA
carbonyl	5	1	iron
cartia	5	1	calcium channel blocker
chorionic	5	1	chorionic gonadotropin intramuscular
desonide	5	1	steroid
diphen	5	1	antihistamine
donnatal	5	1	anticholinergic , antispasmodic , sedative
elppa	5	1	coq10
femhrt	5	1	estrogen , progesterone
Ginkgo Biloba	5	1	Alternative Herbal Medication
imiodium	5	1	loperamide
lysine	5	1	amino acid
miconazole	5	1	azole antifungal
mirabegron	5	1	urinary muscle spasm
oatstraw	5	1	Alternative Herbal Medication
pure	5	1	NA
q3hr	5	1	NA
spots	5	1	NA
valcyte	5	1	cmv antiviral , organ transplant
vinpocetine	5	1	general dementia
atripla	4	1	hiv antiviral
chlorinic	4	1	NA
ciproflaxin	4	1	fluoroquinolone
comtan	4	1	dopamine agonist
depotestosterone	4	1	depo-testosterone
dexlansoprazole	4	1	proton pump inhibitor
dextroamphetamine	4	1	stimulant
dihydroxyaluminum	4	1	antacid
docustate	4	1	stool softener
dorzolamide	4	1	carbonic anhydrase inhibitor
dry	4	1	general cold
dulera	4	1	corticosteroid , long acting beta agonist
entacapone	4	1	dopamine agonist
eplerenone	4	1	potassium-sparing diuretic
etanercept	4	1	blocking tumor necrosi factor alpha

Ex-Lax	4	1	stimulant laxative
feuron	4	1	loop diuretic
gamma	4	1	general alcoholism , general sleep
hfaa	4	1	bronchodilator
imipramine	4	1	general nonopioid , tricyclic antidepressant
integra	4	1	multivitamin
mount	4	1	NA
mounting	4	1	NA
mycaostatin	4	1	nystatin
nadolol	4	1	beta blocker
neutral	4	1	NA
olive	4	1	nutritional supplement
pipen	4	1	NA
polycarbophil	4	1	bulk forming laxative
propecia	4	1	general urinary tract
pumkin	4	1	Alternative Herbal Medication
relpax	4	1	selective serotonin receptor agonist
swallowing	4	1	general excess saliva
taper	4	1	NA
teriparatide	4	1	human parathyroid hormone
tirolony	4	1	support
viread	4	1	hepatitis b antiviral , hiv antiviral
visit	4	1	support
vivix	4	1	polyphenol
zovirax	4	1	progesterone
acebutolol	3	1	beta blocker
air	3	1	NA
asmanex	3	1	corticosteroid
betapace	3	1	beta blocker
bilberry	3	1	Alternative Herbal Medication
caduet	3	1	calcium channel blocker , statin
carisoprolol	3	1	muscle relaxant
chlorpheniramine	3	1	antihistamine
clonidine	3	1	thiazide diuretic
daliresp	3	1	roflumilast
demadex	3	1	loop diuretic
desonate	3	1	corticosteroid

desvenlafaxine	3	1	snri
dramamine	3	1	antihistamine
ears	3	1	general ear
erectile	3	1	NA
exel	3	1	nsaid
fibercon	3	1	bulk forming laxative
gonadotropin	3	1	gonadotropin
gralise	3	1	anticonvulsant , antiepileptic
hydrochlorothiazide	3	1	potassium-sparing diuretic , thiazide diuretic
hydroquinone	3	1	skin bleach
hydroxychloroquine	3	1	anti malarial
jalyn	3	1	alpha-blocker
lab	3	1	NA
lock	3	1	NA
lutein	3	1	carotenoid vitamin
metaxalone	3	1	muscle relaxant
motion	3	1	general motion sicknes
motorized	3	1	NA
moxifloxacin	3	1	quinolone antibiotic
myobloc	3	1	rimabotulinumtoxinb
neomycin	3	1	neomycin
oupatient	3	1	NA
oxymetazoline	3	1	decongestant
paricalcitol	3	1	vitamin d
pen	3	1	NA
perphenazine	3	1	phenothiazine
prilosex	3	1	proton pump inhibitor
psuedobulbar	3	1	ssri
qafternoon	3	1	NA
reclast	3	1	antiresorptive
rizatriptan	3	1	selective serotonin receptor agonist
roho	3	1	skeletal support
serevent	3	1	bronchodilator
sin	3	1	NA
sitagliptin	3	1	dipeptidyl peptidase 4 inhibitor
spacer	3	1	NA
sprinolactone	3	1	potassium-sparing diuretic

sublinguql	3	1	NA
tb	3	1	tb antibiotic
temsulosin	3	1	generl urinary tract
vitafusion	3	1	multivitamin
well	3	1	NA
wheel	3	1	skeletal support
wrist	3	1	NA
alavert	2	1	antihistamine
albuteral	2	1	bronchodilator
amiloride	2	1	potassium-sparing diuretic
aquaphor	2	1	skin ointment
aquatic	2	1	NA
arixtra	2	1	fondaparinux
arthritis	2	1	joint pain
arthrotec	2	1	joint inflammation, nsaid
atacand	2	1	angiotensin ii receptor blocker
azopt	2	1	carbonic anhydrase inhibitor
baclonfen	2	1	muscle relaxant , antispastic
benzonate	2	1	tessalon perle
biloda	2	1	Alternative Herbal Medication
brain	2	1	NA
budesonide	2	1	decongestant , steroid
carbidopa	2	1	dopamine agonist
cardiac	2	1	NA
cardura	2	1	generl urinary tract
catapres	2	1	central alpha agonist
cept	2	1	immunosuppressant
chloraseptic	2	1	analgesic , anesthetic
chlorhexidine	2	1	chlorhexidine gluconate
chloropheniramine	2	1	antihistamine
colon	2	1	general colon
comm	2	1	NA
concerta	2	1	stimulant
creon	2	1	digestive enzyme
cytolopram	2	1	ssri
decreasing	2	1	NA
delatesteryl	2	1	testosterone
dextromethorpha	2	1	cough suppressant
diazepam	2	1	benzodiazepine

diazepam	2	1	benzodiazepine
diltiazem	2	1	calcium channel blocker
diltiazem	2	1	calcium channel blocker
discomfort	2	1	NA
divigil	2	1	bupropion
do	2	1	NA
donepezil	2	1	donepezil
dro	2	1	NA
dynamic	2	1	NA
ear	2	1	general ear
ellipta	2	1	long acting beta agonist
emergency	2	1	NA
ena	2	1	NA
enablex	2	1	muscle spasm
enalpril	2	1	ace inhibitor
enbrel	2	1	blocking tumor necrosis factor alpha
eneteral	2	1	NA
epzicom	2	1	hiv antiviral
esterase	2	1	urine test
ethane	2	1	NA
ethinyl	2	1	estrogen , progestin
ezetimibe	2	1	ezetimibe
fenofibrate	2	1	fibrate
fibrozil	2	1	fibrate
fist	2	1	omega 3
fit	2	1	rectal test
flector	2	1	nsaid
flunisolide	2	1	corticosteroid
forming	2	1	NA
fosfomycin	2	1	fosfomycin tromethamine
Ginkgo Biloba	2	1	Alternative Herbal Medication
glargine	2	1	insulin
gleevec	2	1	small molecule kinase inhibitor
gtt	2	1	NA
guar	2	1	fiber
hh	2	1	support
histussin	2	1	antihistamine , antitussive , decongestant

humalog	2	1	insulin support
hyclate	2	1	tetracycline antibiotic
hydrocone	2	1	opioid
hydrxychloroquine	2	1	anti malarial
hyoscyanime	2	1	anticholinergic , antispasmodic
hyosycamine	2	1	anticholinergic , antispasmodic
hyposcyamine	2	1	anticholinergic , antispasmodic
ibu	2	1	nsaid
ibuprofen	2	1	nsaid
iisinoprol	2	1	ace inhibitor
influenza	2	1	general flu
inhaltion	2	1	NA
insuling	2	1	insulin
intro	2	1	NA
isentress	2	1	antiretroviral
isophane	2	1	insulin
ivermectin	2	1	antiparasitic
juice	2	1	NA
k	2	1	NA
kerlone	2	1	beta blocker
l	2	1	NA
levothyroxin	2	1	levothyroxine
living	2	1	NA
lovaza	2	1	omega 3
macrodantin	2	1	nitrofurantoin
maprotiline	2	1	tricyclic antidepressant
megesterol	2	1	progesterone
memory	2	1	general memory
menthol	2	1	analgesic
meprobamate	2	1	tricyclic antidepressant
meprozine	2	1	antihistamine , opioid
metadata	2	1	NA
metaformin	2	1	high blood sugar control
methylsulfonylm	2	1	methylsulfonylmethane
metoprolol	2	1	beta blocker
metrogel	2	1	metrogel
mexiletine	2	1	anti arrhythmic
midodrine	2	1	midodrine
minoxidil	2	1	minoxidil

monopril	2	1	ace inhibitor
motefil	2	1	immunosuppressant
muir	2	1	NA
musk	2	1	antihistamine , Alternative Herbal Medication
naprozen	2	1	nsaid
naratriptan	2	1	selective serotonin receptor agonists, nsaid
necon	2	1	progesterone , progestin
norfloxacin	2	1	quinolone antibiotic
norvir	2	1	hiv antiviral
ocean	2	1	relaxing
ophthalm	2	1	quinolone antibiotic
orthopedice	2	1	support
ounce	2	1	NA
oxybuynin	2	1	generl urinary tract
pc	2	1	NA
pearl	2	1	multiple possible item
phenytoin	2	1	anticonvulsant
phytosterol	2	1	phytosterol ester
podiatry	2	1	NA
polyunsat	2	1	good fat
polyunsaturated	2	1	good fat
poweder	2	1	skin ointment
powerchair	2	1	skeletal support
pradaxa	2	1	anticoagulant
pravocol	2	1	statin
prefilled	2	1	NA
propantheline	2	1	general ulcer prevention
q24hr	2	1	NA
qamx1month	2	1	NA
quad	2	1	NA
r	2	1	NA
relase	2	1	NA
released	2	1	NA
repetabs	2	1	bronchodilator
resint	2	1	support
risedronate	2	1	antiresorptive
risperidone	2	1	atypical antipsychotic

rivastigmine	2	1	cholinesterase inhibitor
roal	2	1	NA
rubinul	2	1	glycopyrrolate
salicylic	2	1	skin ointment
santyl	2	1	wound dressing
short	2	1	NA
sleepgels	2	1	NA
slp	2	1	statin
sparingly	2	1	NA
speechtherapy	2	1	communication
spironolactone25	2	1	potassium sparing diuretic
spirulina	2	1	multivitamin
sq	2	1	NA
strattera	2	1	atomoxetine hydrochloride , snri
sucralfate	2	1	antacid
tabavite	2	1	iron , multivitamin
tak2	2	1	NA
testium	2	1	scrotum medication , testosterone
throat	2	1	NA
ti	2	1	NA
tibe	2	1	NA
tofranil	2	1	tricyclic antidepressant
tolnaftate	2	1	tolnaftate
tonight	2	1	NA
transdermal	2	1	NA
turmeric	2	1	Alternative Herbal Medication
tussim	2	1	cough suppressant , decongestant , expectorant
twisthaler	2	1	NA
unice	2	1	NA
urecholine	2	1	bethanechol
violet	2	1	gentian violet
viramune	2	1	nnrti
virus	2	1	general antiviral
vitamine	2	1	vitamin e
x4	2	1	NA
xalatan	2	1	latanoprost

you	2	1	NA
zaditor	2	1	antihistamine
zoledronic	2	1	chemotherapy
zomig	2	1	selective serotonin receptor agonists, nsaid
a1	1	1	NA
aam	1	1	NA
abatacept	1	1	abatacept
accupuncture	1	1	acetaminophen
ace	1	1	NA
aceaminophen	1	1	acetaminophen
acetaminiphin	1	1	acetaminophen
acetaminnophen	1	1	acetaminophen
acetaminopehn	1	1	acetaminophen
acetaminphen	1	1	acetaminophen
acit	1	1	NA
aclometasone	1	1	topical steroid
adalat30	1	1	calcium channel blocker
adaptive	1	1	NA
adderal	1	1	stimulant
adult	1	1	NA
adv	1	1	NA
afl	1	1	atrial flutter
aggrenox	1	1	nsaid
ago	1	1	NA
aimlodipine	1	1	calcium channel blocker
alamast	1	1	mast cell stabilizer
albetrol	1	1	bronchodilator
allpurinol	1	1	xanthine oxidase inhibitor
alodipine	1	1	calcium channel blocker
aloe	1	1	Alternative Herbal Medication
alphalipoic	1	1	antioxidant
alprozolam	1	1	benzodiazepine
altropine	1	1	antimuscarinic
alubutanol	1	1	bronchodilator
ambiean	1	1	sedative
amgnesium	1	1	magnesium
amitriptylin	1	1	tricyclic antidepressant
amitryptiline	1	1	tricyclic antidepressant

amoxacillin	1	1	penicillin
amphetamine	1	1	stimulant
ampicillin	1	1	penicillin
amtryptiline	1	1	tricyclic antidepressant
anaprox	1	1	irreversible cyclooxygenase inhibitor
anaspax	1	1	hyoscyamine
anaspaz	1	1	hyoscyamine
anastrozole	1	1	aromatase inhibitor
ancefivpb	1	1	cephalosporin antibiotic
ankle	1	1	NA
antibiotic	1	1	general antibiotic
antidepressant	1	1	general antidepressant
antiemetics	1	1	antihistamine
antihistamine	1	1	antihistamine
antispas	1	1	antispasmodic
antivert	1	1	antihistamine
antoxid	1	1	antioxidant
anxietybaclofen	1	1	antispastic , general anxiety, muscle relaxant
aolpidem	1	1	sedative
apple	1	1	nutritional supplement
aranesp	1	1	darbepoetin alfa
ararax	1	1	hydroxyzine
arbonate	1	1	NA
arjo	1	1	NA
armidex	1	1	nonsteroidal aromatase inhibitor
arivent	1	1	bronchodilator
artane	1	1	dopamine agonist
artificial	1	1	NA
ascorbin	1	1	vitamin c
asipirin	1	1	irreversible cyclooxygenase inhibitor , nsaid
asocorbic	1	1	vitamin c
aspirinm	1	1	irreversible cyclooxygenase inhibitor , nsaid
aspiroin	1	1	irreversible cyclooxygenase inhibitor , nsaid
aspirin	1	1	irreversible cyclooxygenase

			inhibitor , nsaid
atenolol0chlorthalidone	1	1	beta blocker
ativen	1	1	benzodiazepine
atovent	1	1	bronchodilator
atriptan	1	1	nonopioid
atropin	1	1	antimuscarinic
atuss	1	1	antihistamine , cough suppressant , decongestant
avalide	1	1	angiotensin ii receptor blocker
avandia	1	1	glitazone
avaps	1	1	average volume assured pressure support
avinza	1	1	nonopioid
azor	1	1	angiotensin ii receptor antagonist ,calcium channel blocker
bacofen	1	1	antispastic , muscle relaxant
bark	1	1	Alternative Herbal Medication
basis	1	1	NA
bclofen	1	1	antispastic , muscle relaxant
beclamethasone	1	1	corticosteroid
bedtimes	1	1	NA
bee	1	1	NA
benefiber	1	1	wheat dextrin
benicer	1	1	angiotensin receptor blocker
benzapril	1	1	ace inhibitor
berry	1	1	Alternative Herbal Medication
besylate	1	1	calcium channel blocker
betacaotene	1	1	vitamin a
bg	1	1	galectin-3
biacin	1	1	macrolide antibiotic
bictrim	1	1	sulfamethoxazole , trimethoprim
bidm	1	1	NA
bifo	1	1	NA
big	1	1	NA
binant	1	1	NA
bio	1	1	NA
bipsp	1	1	bipap
birth	1	1	NA

bismuth	1	1	bismuth subsalicylate
bisphosphonates	1	1	antiresorptive
bitamin	1	1	multivitamin
ble	1	1	NA
block	1	1	NA
body	1	1	NA
bone	1	1	general bone
boniva	1	1	antiresorptive
bood	1	1	NA
boot	1	1	skeletal support
boswellic	1	1	Alternative Herbal Medication
bottom	1	1	NA
bowel	1	1	general ib
branch	1	1	NA
branched	1	1	NA
breakfast	1	1	nutritional supplement
breo	1	1	corticosteroid , long acting beta agonist
bromide	1	1	anticonvulsant
budeprion	1	1	bupropion
bumetanide	1	1	loop diuretic
bumtanide	1	1	loop diuretic
bupropion	1	1	bupropion
ca	1	1	calcium supplement
ca+	1	1	calcium supplement
caclium	1	1	calcium supplement
calan	1	1	calcium channel blocker
calcitonin	1	1	calcitonin
calciumcarbonate	1	1	calcium supplement
calcium	1	1	calcium supplement
camp	1	1	NA
cantrum	1	1	multivitamin
capex	1	1	steroid
carbamazepine	1	1	anticonvulsant
carbamide	1	1	carbamide peroxide
care	1	1	NA
case	1	1	NA
casodex	1	1	anti androgen
cat's	1	1	NA

catapress	1	1	central alpha agonist
causing	1	1	NA
cefazolin	1	1	cephalosporin antibiotic
ceftin	1	1	cephalosporin antibiotic
cefuroxime	1	1	cephalosporin antibiotic
celexca	1	1	ssri
celexia	1	1	ssri
cenlafaxine	1	1	snri
center	1	1	NA
cephalosporin	1	1	cephalosporin antibiotic
cephalexin	1	1	cephalosporin antibiotic
certainly	1	1	NA
cervical	1	1	cervical cancer
cessation	1	1	smoking cessation medicine
cetirizine	1	1	antihistamine
cetrizine	1	1	antihistamine
cfr	1	1	NA
chamber	1	1	NA
chantix	1	1	smoking cessation medicine
chapter	1	1	NA
check	1	1	NA
chestnut	1	1	NA
chewable	1	1	NA
chews	1	1	NA
childrens	1	1	NA
chlor	1	1	general sleep
chloral	1	1	general sleep
cholesterol	1	1	general heart
chondritin	1	1	chondroitin
chondroitin	1	1	chondroitin
cialopram	1	1	ssri
ciated	1	1	NA
ciatlopram	1	1	ssri
cider	1	1	Alternative Herbal Medication
cimetidine	1	1	general ulcer prevention
citralopram	1	1	ssri
claritin0d	1	1	antihistamine , pseudoephedrine
clavicle	1	1	NA

clay	1	1	NA
cleaning	1	1	NA
cleansing	1	1	NA
clearlax	1	1	osmotic type laxative
clindamycin	1	1	clindamycin
clinical	1	1	NA
clonazepam	1	1	ssri
cloderm	1	1	steroid
clomid	1	1	non-steroidal fertility medicine
clonazepam	1	1	benzodiazepine
clonazepam	1	1	benzodiazepine
cloneazepam	1	1	benzodiazepine
closed	1	1	NA
cm	1	1	NA
coenzyme	1	1	coq10
colase	1	1	stool softener
colazepam	1	1	benzodiazepine
colchicines	1	1	colchicine
cold	1	1	general cold
colesevelam	1	1	bile acid-binding resin
collagenase	1	1	wound dressing
collar	1	1	NA
comfort	1	1	NA
compazine	1	1	proton pump inhibitor
comtex	1	1	acetaminophen , antihistamine , cough suppressant , pseudoephedrine
conazepam	1	1	anticonvulsant , antiepileptic
concentrate	1	1	NA
concurrent	1	1	NA
converted	1	1	NA
coenzyme	1	1	coq10
cope	1	1	stimulant , irreversible cyclooxygenase inhibitor , nsaid
corrective	1	1	NA
cortisone	1	1	hydrocortisone
cosmin	1	1	chondroitin , glucosamine
coumadin	1	1	anticoagulant
country	1	1	NA

cpap	1	1	cpap
cpsule	1	1	NA
creatine	1	1	muscle strengthener
cs	1	1	NA
cuffed	1	1	NA
culcolax	1	1	stimulant laxative
curcumin	1	1	Alternative Herbal Medication
cut	1	1	NA
cyanocobalamin	1	1	vitamin b
cyanovobalamin	1	1	vitamin b
cycle	1	1	NA
cyclobenzprine	1	1	muscle relaxant
cymista	1	1	NA
cypionate	1	1	depo-testosterone
cyproheptadine	1	1	antihistamine
d5w	1	1	dextrose
dailym	1	1	NA
darunavir	1	1	protease inhibitor
darvocett	1	1	opioid
date	1	1	NA
daydulcolax	1	1	stimulant laxative
daypro	1	1	nsaid
decadron	1	1	corticosteroid
december	1	1	NA
decreased	1	1	NA
delica	1	1	NA
dental	1	1	dental help
depending	1	1	NA
dermatology	1	1	NA
desoximetasone	1	1	topical steroid
dessex	1	1	NA
desvenla	1	1	snri
desyrl	1	1	desyrel
detox	1	1	NA
dex	1	1	NA
dexedrine	1	1	stimulant
dexpramipexole	1	1	dexpramipexole
dextrin	1	1	wheat dextrin
dextrol	1	1	generl urinary tract

dextromethoran	1	1	cough suppressant
dextromethorpan	1	1	cough suppressant
dextrose	1	1	dextrose
dhrochlorothiazide	1	1	potassium-sparing diuretic , thiazide diuretic
diclofenax	1	1	nsaid
diclonfenac	1	1	nsaid
dicyclomine	1	1	anticholinergic , antispasmodic
diet	1	1	nutritional supplement
digooxin	1	1	cardiac glycoside
diirected	1	1	NA
diltazem	1	1	calcium channel blocker
diltiazam	1	1	calcium channel blocker
dioval	1	1	progesterone
diphenhydraamine	1	1	antihistamine
diphenhydramin	1	1	antihistamine
diphenoxylate	1	1	anticholinergic
diphyenhydramine	1	1	antihistamine
diprolene	1	1	steroid
discharge	1	1	NA
diuretic	1	1	general diuretic
dmae	1	1	Alternative Herbal Medication
dmso	1	1	generl urinary tract
dnelixir	1	1	NA
docu	1	1	NA
dopa	1	1	dopamine agonist
doryx	1	1	tetracycline antibiotic
dot	1	1	NA
doxepin	1	1	tricyclic antidepressant
dqypro	1	1	nsaid
dr	1	1	NA
drobinol	1	1	marijuana
dsc	1	1	NA
ducosate	1	1	stool softener
dulcolox	1	1	stimulant laxative
duloxetine	1	1	snri
duraphen	1	1	expectorant
durgesic	1	1	opioid
dutasteride	1	1	generl urinary tract

dx	1	1	NA
dymista	1	1	antihistamine
earwax	1	1	general ear
ebteruc	1	1	NA
ec	1	1	NA
eco	1	1	NA
educate	1	1	NA
effector	1	1	snri
EGR/POVI/TNC	1	1	NA
elmiron	1	1	generl urinary tract
else	1	1	NA
elvail	1	1	tricyclic antidepressant
emerita	1	1	NA
emulsion	1	1	NA
enema	1	1	rectal test
energy	1	1	NA
enuretic	1	1	generl urinary tract
epap=10cm	1	1	epap
epipen	1	1	anaphylaxi
episodes	1	1	NA
equate	1	1	antihistamine
equipment	1	1	NA
equivalent	1	1	NA
ergocalcifero	1	1	vitamin d
ergocalcigerol	1	1	vitamin d
escalating	1	1	NA
essential	1	1	NA
esters	1	1	omega 3
estosterone	1	1	testosterone
estrodiol	1	1	estrogen
estrodiol transdermal	1	1	estrogen
estroglmethy	1	1	estrogen , methyltestosterone
ethyl	1	1	omega 3
ex	1	1	stimulant laxative
ex=lax	1	1	stimulant laxative
excedrine	1	1	acetaminophen , stimulant , nsaid
except	1	1	NA
excetrine	1	1	acetaminophen , stimulant ,

			nsaid
excitalopram	1	1	ssri
exemestane	1	1	selective estrogen receptor modulator
experimental	1	1	NA
extension	1	1	NA
eyedrops	1	1	general eye
famotodine	1	1	histamine-2 blocker
fastling	1	1	rectal test
faxed	1	1	NA
feed	1	1	nutritional supplement
feeding	1	1	nutritional supplement
felxeril	1	1	muscle relaxant
fenoprofen	1	1	nsaid
feso4	1	1	iron
fesoterodine	1	1	generl urinary tract
fibuprofen	1	1	nsaid
filsh	1	1	NA
filter	1	1	NA
finger	1	1	NA
flecainide	1	1	anti arrhythmic
flexaril	1	1	muscle relaxant
flexerill	1	1	muscle relaxant
flomac	1	1	generl urinary tract
flu	1	1	general flu
fluid	1	1	nutritional supplement
fluocinolone	1	1	steroid
flush	1	1	NA
flutcasone	1	1	corticosteroid
flutiasone	1	1	corticosteroid
fluticasone propionate	1	1	corticosteroid
foam	1	1	NA
foltx	1	1	hyperhomocysteinemia , vitamin b12 , vitamin b
foradil	1	1	long acting beta agonist
frozen	1	1	NA
fully	1	1	NA
fumarate	1	1	iron
gabapenten	1	1	anticonvulsant , antiepileptic

gabapentin300	1	1	anticonvulsant , antiepileptic
gabepentin	1	1	anticonvulsant , antiepileptic
gait	1	1	NA
gapabentin	1	1	anticonvulsant , antiepileptic
garden	1	1	NA
garlicin	1	1	Alternative Herbal Medication
gay	1	1	NA
generic	1	1	NA
genetic	1	1	NA
genital	1	1	NA
gest	1	1	decongestant , cough medication
get	1	1	NA
glimeriride	1	1	insulin
glucotrol	1	1	insulin
glycerine	1	1	general glaucoma
glycophenylate	1	1	presurgery medication
glycophyrrolate	1	1	anticholinergic
glycopropate	1	1	anticholinergic
glycopyrrolatye	1	1	anticholinergic
glyuburide	1	1	sulfonylurea
gnc	1	1	NA
going	1	1	NA
goji	1	1	Alternative Herbal Medication
gonadotropic	1	1	gonadotropin
gone	1	1	NA
gr	1	1	NA
grapefruit	1	1	Alternative Herbal Medication
greens	1	1	marijuana?
groin	1	1	NA
guabid	1	1	expectorant
Guabid DM	1	1	expectorant
guaifenasin	1	1	expectorant
guaifex	1	1	decongestant , expectorent
guard	1	1	NA
guifenesin	1	1	expectorant
gum	1	1	NA
halcion	1	1	insomnia
haldol	1	1	haloperidol

haloperidol	1	1	haloperidol
hands	1	1	NA
hct80	1	1	angiotensin receptor blocker , potassium-sparing diuretic , thiazide diuretic
healthy	1	1	NA
helath	1	1	NA
hemocyte	1	1	iron
hen	1	1	NA
homeopathic	1	1	Alternative Herbal Medication
homocystine	1	1	folic acid , vitamin b12 , vitamin b6
hormonal	1	1	general hormone
hospice	1	1	support
hot	1	1	NA
hoya	1	1	clinic?
hp	1	1	acetaminophen , opioid
hrm	1	1	NA
hsm	1	1	NA
htcz	1	1	potassium-sparing diuretic , thiazide diuretic
htz	1	1	potassium-sparing diuretic , thiazide diuretic
humulin	1	1	insulin support
huntley	1	1	clinic?
hyaluronic	1	1	hyaluronic acid
hycosamine	1	1	anticholinergic , antispasmodic
hydrate	1	1	water
hydrocodon	1	1	opioid
hydrocondone	1	1	opioid
hydrogen	1	1	NA
hydroxide	1	1	NA
hydroxy	1	1	NA
hydroxyzone	1	1	antihistamine
hylan	1	1	clinic?
hyocodone	1	1	opioid
hyocyamine	1	1	anticholinergic , antispasmodic
hyoscamin	1	1	anticholinergic , antispasmodic
hyoscamine	1	1	anticholinergic , antispasmodic
hyoscyaminee	1	1	anticholinergic , antispasmodic

hypertension	1	1	general heart
hypochlorothiazide	1	1	potassium-sparing diuretic , thiazide diuretic
hypoglycemic	1	1	general hypoglycemia
hypscyamine	1	1	anticholinergic , antispasmodic
hyrdrmorphone	1	1	opioid
hydrocodone	1	1	opioid
hysocyamine	1	1	anticholinergic , antispasmodic
hytrin	1	1	alpha 1 blocker
ib	1	1	NA
ibandronate	1	1	antiresorptive
ibbox	1	1	NA
iexapro	1	1	ssri
ig	1	1	NA
ii	1	1	NA
iisinopril	1	1	ace inhibitor
imatinib	1	1	kinase inhibitor
imdur	1	1	nitrate
immodium	1	1	loperamide
immunoglobulin	1	1	immunoglobulin
immunosuppressant	1	1	immunosuppressant
immunosuppressive	1	1	immunosuppressant
improvements	1	1	NA
inahale	1	1	NA
inahle	1	1	NA
indapamide	1	1	thiazide diuretic
inderal	1	1	beta blocker
ine	1	1	NA
inflamed	1	1	NA
information	1	1	NA
infuse	1	1	NA
inh	1	1	tb antibiotic
inhal	1	1	NA
inhalor	1	1	NA
inhate	1	1	NA
inhlae	1	1	NA
inhlation	1	1	NA
initial	1	1	NA
initially	1	1	NA

inj	1	1	NA
inner	1	1	NA
insomnia	1	1	general sleep
insulin	1	1	insulin
intermittent	1	1	NA
international	1	1	NA
intravenously	1	1	NA
intrex	1	1	selective serotonin receptor agonist
iopidine	1	1	alpha-adrenergic agonist
loratadine	1	1	antihistamine
ipap	1	1	NA
iplex	1	1	igf 1 , peripheral neuropathy
irak	1	1	immunosuppressant
irbesartan	1	1	angiotensin ii receptor antagonist
isosource	1	1	nutritional supplement
itamin	1	1	vitamin
itnl	1	1	NA
IV Solumedrol	1	1	nutritional supplement
jantoven	1	1	anticoagulant
jfa	1	1	NA
joint	1	1	general joint health
kci	1	1	potassium
kenalog	1	1	corticosteroid
kennesaw	1	1	support
keppra	1	1	anticonvulsant , antiepileptic
ketaprofen	1	1	nsaid
ketoconazole	1	1	azole antifungal
ketoprofen	1	1	nsaid
ketorolac	1	1	nsaid
kidney	1	1	NA
klonopin	1	1	benzodiazepine
klor M	1	1	potassium
knee	1	1	NA
know	1	1	NA
kona	1	1	support
lOtryptophan	1	1	amino acid
lactase	1	1	lactose intolerance

lacto	1	1	lactose intolerance
lamotrigine	1	1	antiepileptic
lanoxin	1	1	cardiac glycoside
last	1	1	NA
lax	1	1	general constipation
leaf	1	1	NA
legs	1	1	NA
lescol	1	1	statin
levbid	1	1	anticholinergic , antispasmodic
level	1	1	NA
levemir	1	1	insulin detemir
levmetafetamine	1	1	decongestant
levmetamfetamine	1	1	decongestant
levocarnitine	1	1	levocarnitine
levocetirizine	1	1	antihistamine
levofloxacin	1	1	quinolone antibiotic
levothyroxine	1	1	levothyroxine
levothyrozine	1	1	levothyroxine
lexampro	1	1	ssri
lexaro	1	1	ssri
librax	1	1	anticholinergic , antispasmodic , benzodiazepine
linzess	1	1	linaclotide
lipocential	1	1	drug company
lisinoprial	1	1	ace inhibitor
lisinoprol	1	1	ace inhibitor
lisinipril	1	1	ace inhibitor
list	1	1	NA
listed	1	1	NA
lite	1	1	NA
livalo	1	1	statin
loasartan	1	1	angiotensin ii receptor antagonist
local	1	1	NA
lodipine	1	1	calcium channel blocker
lomotil	1	1	antidiarrheal , antimuscarinic
lorasepam	1	1	benzodiazepine
loratan	1	1	acetaminophen , opioid
loratidine	1	1	antihistamine

loraxepam	1	1	benzodiazepine
lorazepan	1	1	benzodiazepine
lorazepum	1	1	benzodiazepine
lorazpam	1	1	benzodiazepine
lorsarttan	1	1	angiotensin ii receptor antagonist
lortrel	1	1	ace inhibitor
lotrimin	1	1	azole antifungal
loyer	1	1	NA
lozenge	1	1	anesthetic
lrtab	1	1	opioid
ls	1	1	lichen sclerosis
lupron	1	1	synthetic gonadotropin releasing hormone
lyme	1	1	lyme disease
m20	1	1	NA
magnesium hydroxide	1	1	magnesium
maint	1	1	NA
maintain	1	1	NA
major	1	1	NA
make	1	1	NA
many	1	1	NA
maspan	1	1	nutritional supplement
massage	1	1	stres relief
mayo	1	1	clinic?
mda	1	1	NA
means	1	1	NA
mechanical	1	1	NA
medidation	1	1	NA
medrol	1	1	adrenocortical steroid
meidcation	1	1	NA
menocycline	1	1	tetracycline antibiotic
menstrual	1	1	general hormone
mental	1	1	NA
mentioned	1	1	NA
mestonin	1	1	pyridostigmine
metaclopramide	1	1	metoclopramide
metadate	1	1	NA
metal	1	1	NA

methycellulose	1	1	bulk forming laxative
methyldopa	1	1	antihypertensive
methysulfonylm	1	1	methysulfonylmethane
metoclopr	1	1	metoclopramide
metoclopramid	1	1	metoclopramide
metoprolol	1	1	beta blocker
metopropol	1	1	beta blocker
metopropol	1	1	beta blocker
miacalcin	1	1	miacalcin
midgraine	1	1	general head pain
milliequivalents	1	1	NA
milligrams	1	1	NA
minicycline	1	1	tetracycline antibiotic
minimal	1	1	NA
minipress	1	1	alpha adrenergic blocker
mirabergron	1	1	urinary muscle spasm
miralaz	1	1	osmotic type laxative
mirapex1	1	1	dopamine agonist
mirtazapin	1	1	mirtazapine
misoprostol	1	1	abortion pill
mitochondria	1	1	general mitochondrial
mitochondrial	1	1	general mitochondrial
mloral	1	1	NA
mls	1	1	NA
mm	1	1	NA
mode	1	1	NA
modeafinil	1	1	awakefullnes
mom	1	1	support
monocycline	1	1	tetracycline antibiotic
mood	1	1	general antidepressant
more	1	1	NA
motor	1	1	NA
mp	1	1	NA
mri	1	1	magnetic resonance imaging
msir	1	1	morphine
mstinon	1	1	pyridostigmine
mtx	1	1	antimetabolite
mucofen	1	1	cough suppressant , expectorant

muedexta	1	1	stimulant
multifocal	1	1	NA
multivitamin	1	1	multivitamin
mupirocine	1	1	antibacterial , mupirocin
muscinex	1	1	cough suppressant , expectorant
muscular	1	1	general muscle
myasthenia	1	1	general myasthenia gravi
mycelex	1	1	azole antifungal
Mycelex Troche	1	1	azole antifungal
mycopenolate	1	1	immunosuppressant
mycostatin	1	1	nystatin
mylicon	1	1	simethicone
mysoline	1	1	anticonvulsant
mytab	1	1	simethicone
nac	1	1	acetylcysteine
naftin	1	1	naftifine
nano	1	1	NA
naprelan	1	1	nsaid
naprosen	1	1	nsaid
naproxin	1	1	nsaid
nasarel	1	1	corticosteroid
natural	1	1	NA
naturals	1	1	NA
natures	1	1	NA
nebivolol	1	1	beta blocker
nebulized	1	1	NA
ned	1	1	NA
neded	1	1	NA
need	1	1	NA
neostigmine	1	1	neostigmine bromide
neupro	1	1	dopamine agonist
neupro	1	1	dopamine agonist
neurotin	1	1	anticonvulsant
neurotonin	1	1	anticonvulsant
neutropenia	1	1	neutropenia
never	1	1	NA
nexlum	1	1	proton pump inhibitor
nfr2	1	1	antioxidant

ngiht	1	1	NA
nhc	1	1	support
nifedical	1	1	calcium channel blocker
nigf	1	1	brain cancer
nipp	1	1	cephalosporin antibiotic
nisoldipine	1	1	calcium channel blocker
nitrofurantoin	1	1	nitrofurantoin
nontriptyline	1	1	tricyclic antidepressant
nor	1	1	progestin
nordic	1	1	support
nortripyline	1	1	tricyclic antidepressant
norvascm	1	1	calcium channel blocker
nostril	1	1	decongestant
noted	1	1	NA
nothing	1	1	NA
novacort	1	1	anesthetic
novasource	1	1	muscle strengthener
now	1	1	NA
nuleb	1	1	nsaid
number	1	1	NA
nutracalm	1	1	multivitamin
o	1	1	NA
olanzapine	1	1	atypical antipsychotic
om	1	1	NA
omeprazole	1	1	general gastro , proton pump inhibitor
omeprozole	1	1	general gastro , proton pump inhibitor
omnicef	1	1	cephalosporin antibiotic
omperizole	1	1	general gastro , proton pump inhibitor
onadotropin	1	1	NA
onset	1	1	NA
opana	1	1	opioid
ophtahlmic	1	1	quinolone antibiotic
orad	1	1	NA
oralcapsule	1	1	NA
oratablet	1	1	NA
orchard	1	1	support

order	1	1	NA
oreal	1	1	NA
oregano	1	1	nutritional supplement
orencia	1	1	immunosuppressant
organic	1	1	NA
orthopedic	1	1	support
oth	1	1	NA
otic	1	1	quinolone antibiotic
otpatient	1	1	support
out	1	1	NA
outbursts	1	1	NA
oxadol	1	1	nefopam hydrochloride
oxandrine	1	1	anabolic steroid
oxaprozin	1	1	nsaid
oxazepam	1	1	benzodiazepine
oxy10	1	1	skin antibiotic
oxybutrin	1	1	antispasmodic
oxycodone	1	1	opioid
oxycontin80	1	1	opioid
oxycontin	1	1	opioid
oxydose	1	1	opioid
oxygen	1	1	NA
oz	1	1	NA
pa	1	1	NA
pacil	1	1	ssri
package	1	1	NA
pak	1	1	NA
pam	1	1	NA
pancreas	1	1	general gastro
pantaprazole	1	1	proton pump inhibitor
pantothenic	1	1	vitamin b
pantprazole	1	1	proton pump inhibitor
papaya	1	1	nutritional supplement
paraneoplastic	1	1	paraneoplastic disorder
paroxetine	1	1	ssri
parsitan	1	1	ethopropazine
passy	1	1	NA
paste	1	1	NA
patanol	1	1	antihistamine

Patanol ophthalmic	1	1	antihistamine
patassium	1	1	potassium
patches	1	1	NA
pathology	1	1	NA
patient	1	1	NA
patients	1	1	NA
pavastatin	1	1	statin
pe	1	1	NA
ped	1	1	NA
peginterferon	1	1	peginterferon alfa-2a
peptobismol	1	1	bismuth subsalicylate
percordan	1	1	nsaid , opioid
perciset	1	1	acetaminophen , opioid
perhenazine	1	1	phenothiazine
periactin	1	1	antihistamine
pericolace	1	1	stool softener and laxative
peridex	1	1	antimicrobial
period	1	1	NA
pharmacy	1	1	NA
pharyngitis	1	1	acute pharyngiti antiviral
phenergaan	1	1	antihistamine , general nausea , general vomiting , sedative , promethazine
phenergnan	1	1	antihistamine , general nausea , general vomiting , sedative , promethazine
phenobarb	1	1	barbiturate
phenylephrine	1	1	decongestant
phs	1	1	NA
pilocarpine	1	1	anticholinergic
pine	1	1	Alternative Herbal Medication
pioglitazone	1	1	thiazolidinedione
piroxicam	1	1	nsaid
pitavastatin	1	1	statin
placed	1	1	NA
placement	1	1	NA
plan	1	1	NA
planned	1	1	NA
plans	1	1	NA

plant	1	1	Alternative Herbal Medication
plendil	1	1	calcium channel blocker
pntoprazole	1	1	proton pump inhibitor
polgraf	1	1	NA
pollen	1	1	general allergie
poluunsaturated	1	1	good fat
polyunsaturate	1	1	good fat
pomegranet	1	1	nutritional supplement
poqd	1	1	NA
pormula	1	1	nutritional supplement
porzac	1	1	ssri
possibly	1	1	NA
post	1	1	NA
potasium	1	1	potassium
potasium chloride	1	1	potassium
potentially	1	1	NA
povigil	1	1	modafinil
pox5	1	1	benzodiazepine
poyunsaturated	1	1	good fat
ppd	1	1	NA
prazole	1	1	proton pump inhibitor
prdenisone	1	1	corticosteroid
pre	1	1	NA
precaution	1	1	NA
predisone	1	1	corticosteroid
prednsione	1	1	corticosteroid
pregnenolone	1	1	pregnenolone
prenatal	1	1	multivitamin
presumptive	1	1	NA
pretty	1	1	NA
prev	1	1	NA
prevastatin	1	1	statin
previous	1	1	NA
prilozec	1	1	proton pump inhibitor
primal	1	1	NA
problems	1	1	NA
progesterone	1	1	progesterone
prometrium	1	1	progestin
promises	1	1	NA

propionate	1	1	nasal steroid
pseudoephedrine	1	1	decongestant
ptch	1	1	NA
puffer	1	1	NA
pulmonary	1	1	NA
pulmonicort	1	1	corticosteroid
pumps	1	1	NA
q10am	1	1	coq10
q12	1	1	NA
q3	1	1	NA
q3days	1	1	NA
q406hrs	1	1	NA
q4wk	1	1	NA
q5	1	1	NA
q50	1	1	NA
q5ming	1	1	NA
q6h4	1	1	NA
q7	1	1	NA
q8am	1	1	NA
q8r	1	1	NA
qdaily	1	1	NA
qday30	1	1	NA
qh	1	1	NA
qnoon	1	1	NA
qotherd	1	1	NA
quaifenasin	1	1	expectorant
quanfacine	1	1	guanfacine
questran	1	1	bile acid binding resin
quinidin	1	1	anti arrhythmic
quinine324mg	1	1	quinine
qunidine	1	1	qunidine
qvar	1	1	NA
ral	1	1	support
raloxifene	1	1	testosterone
ramadol	1	1	opioid
rampril	1	1	ace inhibitor
rantidine	1	1	histamine 2 blocker
rate	1	1	NA
received	1	1	NA

recom	1	1	NA
recover	1	1	NA
recovered	1	1	NA
reduced	1	1	NA
reg	1	1	NA
regimen	1	1	NA
registered	1	1	NA
reishi	1	1	Alternative Herbal Medication
rejected	1	1	NA
releive	1	1	NA
relutec	1	1	als treatment
remember	1	1	NA
repair	1	1	NA
repeat	1	1	NA
restasis	1	1	immunosuppressant
retin	1	1	vitamin a
return	1	1	NA
reyataz	1	1	protease inhibitor
rhonocort	1	1	budesonide , corticosteroid
rhythmol	1	1	anti arrhythmic
ribavirin	1	1	peginterferon alfa 2a , peginterferon alpha 2b
riboflavin	1	1	vitamin b
rifampin	1	1	tb antibiotic
rilogy	1	1	support
rite	1	1	rite aid
rituximab	1	1	monoclonal antibody
rivaroxaban	1	1	rivaroxaban
robamol	1	1	glycopyrrolate
robinual	1	1	general ulcer prevention
robinuls	1	1	general ulcer prevention
rocephin	1	1	cephalosporin antibiotic
rolling	1	1	NA
room	1	1	NA
rosiglitazone	1	1	thiazolidinedione
rosuvastatin10	1	1	statin
rounds	1	1	NA
routine	1	1	NA
rozeram	1	1	ramelteon

rpn	1	1	support
rx	1	1	NA
saltrophine	1	1	anticholinergic
savella	1	1	snri
scale	1	1	NA
scalp	1	1	NA
scopalamine	1	1	antisecretion
scopolamin	1	1	scopolamine
seborrheic	1	1	seborrheic dermatiti
second	1	1	NA
send	1	1	NA
sennakot	1	1	stimulant laxative
senns	1	1	stimulant laxative
seoquel	1	1	atypical antipsychotic
seroque	1	1	atypical antipsychotic
sertraline200mg	1	1	ssri
serzone	1	1	nefazodone
set	1	1	NA
shake	1	1	NA
shepard	1	1	support
shiley	1	1	NA
shortnes	1	1	NA
sial	1	1	support
sialorrhea	1	1	general exces saliva
siberian	1	1	eleutheroside
sicontinue	1	1	NA
significant	1	1	NA
silvadene	1	1	antimicrobial
silvadine	1	1	antimicrobial
silve	1	1	silver
simbastatin	1	1	statin
simva	1	1	statin
sinamet	1	1	carbidopa , levodopa
sitrate	1	1	sodium salt
sk	1	1	NA
skeleton	1	1	NA
skin	1	1	skin ointment
sleeping	1	1	general sleep
slowly	1	1	NA

small	1	1	NA
snif	1	1	support
sodiumum	1	1	sodium salt
sofran	1	1	ondansetron
softner	1	1	stool softener
solaray	1	1	NA
solid	1	1	NA
solumedrol	1	1	steroid , anti inflammatory
sonne	1	1	NA
spansule	1	1	stimulant
spasms	1	1	general muscle spasm
spasticity	1	1	general muscle spasm
speaking	1	1	communication
spine	1	1	NA
splints	1	1	skeletal support
springkles	1	1	divalproex sodium
sprinkles	1	1	divalproex sodium
spriva	1	1	bronchodilator
sqare	1	1	NA
starter	1	1	NA
startin	1	1	statin
statin	1	1	statin
stedy	1	1	NA
stocking	1	1	compression stocking
straline	1	1	ssri
strenghttylenol	1	1	acetaminophen
stress	1	1	general anxiety
stretching	1	1	NA
subcu	1	1	NA
subcuan	1	1	NA
subsequently	1	1	NA
substitutes	1	1	NA
subutaneous	1	1	NA
such	1	1	NA
sucralyate	1	1	sucralfate
sufate	1	1	iron
sugar	1	1	NA
sular	1	1	calcium channel blocker
sulfamethoxazole	1	1	sulfamethoxazole ,

			trimethoprim
sun	1	1	vitamin d
supplementation	1	1	NA
supplies	1	1	NA
suppository	1	1	NA
sustained	1	1	NA
swish	1	1	nystatin
symptoms	1	1	NA
synthoid	1	1	levothyroxine
synthrooid	1	1	levothyroxine
synthroid	1	1	levothyroxine
syntrhoid	1	1	levothyroxine
ta	1	1	NA
tables	1	1	NA
tablete	1	1	NA
tablie	1	1	NA
tabpo	1	1	NA
tacromilus	1	1	organ donation
tagamet	1	1	general ulcer prevention
tam	1	1	NA
tamezapan	1	1	general sleep
tamoxifen	1	1	tamoxifen
tavkete	1	1	NA
tbs	1	1	NA
teaspon	1	1	NA
tech	1	1	NA
tegretol	1	1	anticonvulsant
teice	1	1	NA
tell	1	1	communication
temp	1	1	NA
tenormin	1	1	beta blocker
tetracycline	1	1	tetracycline antibiotic
tev	1	1	angiotensin ii receptor antagonist
therapies	1	1	NA
theratears	1	1	ocular lubricant
thistle	1	1	milk thistle
throid	1	1	general hypothyroidism
thru	1	1	NA

thursday	1	1	NA
thyroxine	1	1	anhydrous_levothyroxine_sodium
tib	1	1	NA
timoptic	1	1	beta blocker
tims	1	1	NA
tinea	1	1	tinea cruri
tiotropiu	1	1	anticholinergic
tips	1	1	NA
titration	1	1	NA
titrations	1	1	NA
tizanadine	1	1	muscle relaxant
tizandine	1	1	muscle relaxant
tizanide	1	1	muscle relaxant
tiziaz	1	1	NA
tobradex	1	1	steroid , tobramycin
Tolterodine Tartrate	1	1	generl urinary tract
tomes	1	1	NA
tonic	1	1	NA
took	1	1	NA
toproixl	1	1	beta blocker
tor	1	1	potassium sparing diuretic
torol	1	1	beta blocker
torsmeide	1	1	potassium sparing diuretic
touch	1	1	NA
toviaz	1	1	bladder relaxant
tr	1	1	NA
tracheostomy	1	1	tracheostomy tube
tradjenta	1	1	linagliptin
tradzodone	1	1	trazedone
tramodol	1	1	analgesic
transderaml	1	1	NA
transfermal	1	1	NA
transmucosal	1	1	NA
trazodine	1	1	trazedone
trazone	1	1	trazedone
treat	1	1	NA
treated	1	1	NA
treatments	1	1	NA

trezadone	1	1	trazedone
triamclinoline	1	1	topical steroid
trimethobenzamide	1	1	antihistamine
trimethoprim	1	1	trimethoprim
trimeton	1	1	antihistamine
triolgy	1	1	support
triology	1	1	NA
troglitazone	1	1	antihyperglycemic
trosipium	1	1	generl urinary tract
Trosipium Chloride	1	1	generl urinary tract
trough	1	1	NA
truvada	1	1	nrti
trying	1	1	NA
tryptophan	1	1	Alternative Herbal Medication
tub	1	1	NA
tussin	1	1	cough suppressant , decongestant , expectorant
tv	1	1	NA
twe	1	1	NA
twelve	1	1	NA
tyelonol	1	1	nonopioid
tyenol	1	1	nonopioid
type	1	1	NA
tz	1	1	quinolone antibiotic
u10	1	1	NA
u20	1	1	NA
ubiquinine	1	1	coq10
ubtl	1	1	NA
ue	1	1	NA
ug	1	1	NA
ui	1	1	NA
ulcerative	1	1	ulcerative coliti
ultracet	1	1	acetaminophen , tramadol
uncertain	1	1	NA
undetermined	1	1	NA
unsaturated	1	1	good fat
untl	1	1	NA
untoward	1	1	NA
update	1	1	NA

upwards	1	1	NA
uroquid	1	1	urinary tract antibiotic
uroxatral	1	1	corticosteroid
uses	1	1	NA
usually	1	1	NA
vaccine	1	1	NA
valong	1	1	support
valproic	1	1	antiepileptic
valstartan	1	1	angiotensin ii receptor antagonist
valtrax	1	1	herpe antiviral
vancomycin	1	1	vancomycin
varenicline	1	1	varenicline
varies	1	1	NA
vasculera	1	1	diosmiplex
vasculitis	1	1	vasculiti
venlafaxin	1	1	snri
venlafazine	1	1	snri
vent	1	1	decongestant , expectorant
ventilator	1	1	mechanical ventilator
veramyst	1	1	corticosteroid
verapmil	1	1	calcium channel blocker
verpamil	1	1	calcium channel blocker
viactiv	1	1	calcium supplement , vitamin d
vials	1	1	NA
viatamin	1	1	NA
viatmin	1	1	NA
vicodan	1	1	acetaminophen , opioid
vicoden	1	1	acetaminophen , opioid
vicon	1	1	multivitamin
vicoprofen	1	1	nsaid , opioid
viden	1	1	NA
vigamox	1	1	quinolone antibiotic
vilazodone	1	1	ssri
vinegar	1	1	nutritional supplement
virtamin	1	1	NA
vita	1	1	vitamin a
vital	1	1	NA
vitamen	1	1	vitamin

vitamin b100	1	1	vitamin b
vitamin b6	1	1	vitamin b
vitamin e4000	1	1	vitamin e
voltarent	1	1	nsaid
vomiting	1	1	NA
vyvancse	1	1	stimulant
walker	1	1	skeletal support
waltussin	1	1	expectorant
warrior	1	1	Alternative Herbal Medication
watching	1	1	NA
ways	1	1	NA
weak	1	1	NA
wearing	1	1	NA
welbutrin	1	1	bupropion , smoking cessation medicine
wellburtrin	1	1	bupropion
went	1	1	NA
were	1	1	NA
wheezing	1	1	general breathing
whey	1	1	muscle strengthener
while	1	1	NA
why	1	1	NA
wice	1	1	NA
wide	1	1	NA
withdrawal	1	1	NA
without	1	1	NA
wk	1	1	NA
wort	1	1	purpose
would	1	1	NA
wresting	1	1	NA
x2	1	1	NA
xanaflex	1	1	muscle relaxant
xanex	1	1	benzodiazepine
xango	1	1	nutritional supplement
xe	1	1	beta blocker
xonpenex	1	1	brochospasm
xopene	1	1	brochospasm
xoponox	1	1	brochospasm
xymogen	1	1	Alternative Herbal Medication

years	1	1	NA
zanaflax	1	1	muscle relaxant
zanax	1	1	benzodiazepine
zemplar	1	1	vitamin d
zero	1	1	NA
Ziac	1	1	beta blocker , diuretic , thiazide diuretic
zofram	1	1	ondansetron
zoladex	1	1	goserelin
zonegran	1	1	anticonvulsant
zooloft	1	1	ssri
zyprexa	1	1	atypical antipsychotic

APPENDIX B

Full Table 3: Individual Medications, number of people taking them, number of visits when they were being taken, and intervention categories the medication belongs to.

Intervention Category	# of Patients	# of Visits
support	972	2722
Rilutek	945	2874
nsaid	661	1685
stimulant	646	1703
stimulant laxative	641	1663
nutritional supplement	618	1528
vitamin	565	1499
calcium supplement	555	1464
ssri	524	1494
opioid	516	1276
vitamin a	475	1241
ace inhibitor	469	1218
benzodiazepine	440	1203
diuretic	422	1015
potassium	413	983
beta blocker	394	1004
omega 3	371	986
multivitamin	359	888
statin	346	844
antispastic	340	1150
general sleep	322	767
irreversible cyclooxygenase inhibitor	319	774
antihistamine	313	735
proton pump inhibitor	290	700
calcium channel blocker	287	737
acetaminophen	282	631
feeding tube	266	517
Alternative Herbal Medication	246	510

steroid	225	541
potassium-sparing diuretic	213	495
potassium sparing diuretic	212	457
thiazide diuretic	211	491
anticonvulsant	208	498
corticosteroid	201	484
anticholinergic	199	433
vitamin b	187	431
expectorant	186	367
general urinary tract	179	447
nonopioid	179	362
muscle relaxant	173	448
antiepileptic	170	433
decongestant	167	318
levothyroxine	154	463
vitamin d	153	366
general hypothyroidism	149	441
antinuclear antibody	141	322
quinolone antibiotic	140	233
antacid	138	244
bronchodilator	132	368
skin ointment	130	272
sedative	129	304
general gastro	128	261
vitamin e	124	325
stool softener	123	258
tricyclic antidepressant	120	304
angiotensin receptor blocker	117	218
coq10	114	229
urinary tract infection antibiotic	113	249
angiotensin ii receptor antagonist	112	274
tb antibiotic	110	260
vitamin c	110	295
lichen sclerosus	108	250
progestin	101	210
good fat	99	220
general ulcer prevention	98	180
antispasmodic	96	182
sublingual	94	160

cough suppressant	93	169
iron	93	187
histamine-2 blocker	92	232
sleep problem	92	183
anhydrous_levothyroxine_sodium	87	223
insulin	86	219
osmotic type laxative	83	147
general constipation	82	145
general flu	81	170
muscle strengthener	81	155
snri	80	224
analgesic	79	174
test	78	144
vision loss, pain, fatigue, and impaired coordination	78	207
anticoagulant	77	173
loop diuretic	76	174
lower blood sugar level	76	227
range of motion	74	139
magnesium	72	150
estrogen	70	147
general cough	66	120
quinine	66	146
adp receptor inhibitor	60	115
hypnotic	59	139
progesterone	59	120
dopamine agonist	58	154
trazedone	58	157
general exces saliva	54	101
atrial flutter	53	118
immunosuppressant	53	168
pyridostigmine	51	78
suction machine	48	88
bupropion	47	144
serotonin	47	120
chondroitin	46	116
fibrate	46	103
general anxiety	46	74
long acting beta agonist	45	128

general nausea	44	75
glucosamine	44	107
antipsychotic	43	84
testosterone	43	89
antimuscarinic	41	66
antiresorptive	41	90
tetracycline antibiotic	40	74
alpha blocker	39	110
acetylcysteine	38	82
general cold	37	66
fluoroquinolone	36	57
skeletal support	36	66
atypical antipsychotic	35	75
bulk forming laxative	35	69
scopolamine	35	57
silver	35	77
ezetimibe	34	70
marijuana	34	75
marijuana?	34	75
antioxidant	33	59
metoclopramide	33	67
muscle spasm	33	74
patient lift	33	48
xanthine	33	77
antiplatelet	32	64
azole antifungal	31	46
general antiplatelet	31	63
cough medication	30	47
general eye	30	50
general vomiting	30	56
bipap	29	49
general m	29	51
norepinephrine reuptake inhibitor	29	71
trimethoprim	29	60
organ donation	28	109
purpose	28	63
als treatment	26	33
anti arrhythmic	26	79

sulfamethoxazole	26	57
cephalosporin	25	40
cephalosporin antibiotic	25	40
nitrate	25	58
ondansetron	25	58
xanthine oxidase inhibitor	25	62
communication	24	45
general breathing	24	33
rectal test	23	36
general antibiotic	22	36
penicillin	22	29
zinc supplement	22	41
amino acid	21	33
anesthetic	21	31
general muscle	21	35
lactose intolerance	21	41
mirtazapine	21	44
nystatin	21	37
phosphodiesterase inhibitor	21	58
niacin	20	48
selective serotonin receptor agonist	20	51
angiotensin ii receptor blocker	19	38
cardiac glycoside	19	59
carbidopa	18	51
general ear	18	28
general muscle spasm	18	32
glitazone	18	36
leukotriene inhibitor	18	47
levodopa	18	51
n-methyl-d-aspartate-receptor antagonist	18	42
botox	17	27
donepezil	17	43
awakefullnes	16	32
general heart	16	17
selective serotonin receptor agonists, nsaid	16	40
simethicone	16	28

antitussive	15	42
water	15	18
insulin glargine	14	27
vasodilator	14	24
fiber	13	32
general allergie	13	26
herpe antiviral	13	38
promethazine	13	14
topical steroid	13	23
colonic acidifier	12	27
exercise	12	26
hydrocortisone	12	26
immunoglobulin	12	13
tessalon perle	12	21
cramp	11	22
general head pain	11	27
insulin support	11	14
methysulfonylmethane	11	49
tadalafil	11	27
thiazolidinedione	11	24
urinary muscle spasm	11	33
antidiarrheal	10	18
average volume assured pressure support	10	18
loperamide	10	29
prostaglandin analog	10	26
anti inflammatory	9	13
antimanic	9	13
pseudoephedrine	9	12
ropinirole	9	15
selective estrogen receptor modulator	9	10
sulfonylurea	9	21
tumour necrosi factor	9	15
brochospasm	8	20
cmv antiviral	8	30
dutasteride	8	18
enoxaparin sodium	8	11
general antidepressant	8	8

macrolide type antibiotic	8	10
organ transplant	8	30
antipruritic agent	7	11
carotenoid vitamin	7	14
clindamycin	7	9
colchicine	7	14
general sinus	7	8
general bone	7	15
general hormone	7	9
glycopyrrolate	7	8
methyltestosterone	7	19
alpha 1 blocker	6	10
aminosalicylate	6	14
bile acid	6	6
blood pressure	6	6
chemotherapy	6	13
contrast agent	6	15
dipeptidyl peptidase 4 inhibitor	6	13
latanoprost	6	11
leukotriene receptor antagonist	6	15
liver test	6	9
nitrofurantoin	6	14
nitroimidazole	6	10
smoking cessation medicine	6	8
wheat dextrin	6	9
adrenocortical steroid	5	5
alpha adrenergic blocker	5	15
alpha agonist	5	19
blocking nerve impulse	5	8
budesonide	5	14
clinic?	5	6
contraceptive	5	9
hiv antiviral	5	14
lactobacillu	5	8
milk thistle	5	9
monoclonal antibodie	5	11
opiate antagonist	5	16
tamoxifen	5	6
anti malarial	4	10

antimetabolite	4	13
aromatase inhibitor	4	12
bile acid binding resin	4	4
blocking tumor necrosi factor alpha	4	9
carbonic anhydrase inhibitor	4	15
glycopyrrolate_	4	4
gonadotropin	4	14
joint inflammation	4	7
linaclotide	4	8
lumigan ophthalmic	4	8
magnetic resonance imaging	4	8
phosphate inhibitor	4	7
tracheostomy tube	4	5
triamcinolone acetonide	4	4
ursodiol	4	6
varденаfil	4	17
aminoglycoside antibiotic	3	3
anti androgen	3	9
antiflatulent	3	3
antihypertensive	3	3
antisecretion	3	3
azithromycin	3	10
barbiturate	3	6
bismuth subsalicylate	3	4
botulinum toxin	3	6
chloride channel activator	3	9
copper	3	7
cpap	3	7
dementia and alzheimer' disease.	3	6
doxylamine	3	17
general ib	3	3
general mitochondrial	3	3
general nonopioid	3	6
haloperidol	3	3
hydroxyzine	3	4
influenza a antiviral	3	7
joint pain	3	4
mesenteric venou thrombosi	3	4

metrogel	3	7
metronidazole	3	10
miacalcin	3	6
monoclonal antibody	3	4
nasal steroid	3	9
nippv	3	4
parkinson' disease	3	3
skeletal muscle troponin activator	3	3
thyroid medication	3	5
triiodothyronine	3	4
wound dressing	3	6
yeast infection treatment	3	6
acupuncture	2	2
anabolic steroid	2	2
antimicrobial	2	3
antiseptic	2	2
apoeaquorin	2	5
atomoxetine hydrochloride	2	4
bladder relaxant	2	2
calcitonin	2	5
cancer treatment	2	4
cenestin	2	2
central alpha agonist	2	6
cervical cancer	2	3
complete blood count	2	3
cortisol	2	2
dental help	2	5
depo-testosterone	2	5
desyrel	2	3
dextrose	2	2
divalproex sodium	2	2
drug helper	2	13
epap	2	2
expectorent	2	2
general asthma	2	2
general dementia	2	9
general diuretic	2	2
general glaucoma	2	2
guanfacine	2	9

histamine 2 blocker	2	2
hormone replacement therapy	2	8
hyaluronic acid	2	2
hyoscyamine	2	2
hypochloremia test	2	2
inclusion body myositi drug	2	4
insulin detemir	2	13
macrolide antibiotic	2	2
mast cell stabilizer	2	3
mechanical ventilator	2	7
metformin	2	4
methylprednisolone	2	2
midodrine	2	4
minoxidil	2	3
nefazodone	2	3
neostigmine bromide	2	2
nrti	2	3
ovarian hyperstimulation	2	4
oxybutynin	2	2
peripheral neuropathy	2	2
phenothiazine	2	5
plcae?	2	2
prevacid	2	2
protease inhibitor	2	2
resveratrol	2	2
rivaroxaban	2	2
selenium	2	4
sodium salt	2	2
strep throat	2	2
synthetic gonadotropin releasing hormone	2	5
tegaserod	2	4
terbinafine hydrochloride	2	3
tobramycin	2	2
tramadol	2	4
vancomycin	2	5
varenicline	2	2
vitamin b12	2	2
vitamin k	2	4

vomit inducer	2	2
zoster vaccine	2	2
abatacept	1	5
abortion pill	1	1
acute pharyngiti antiviral	1	1
alpha-adrenergic agonist	1	1
alpha-adrenergic blocker	1	1
alpha-blocker	1	4
alpha-ketoglutarate	1	5
analgesic pain reliever	1	1
anaphylaxi	1	4
anti anginal medication	1	2
antibacterial	1	1
antihyperglycemic	1	1
antipanic	1	1
antiparasitic	1	2
antiretroviral	1	2
arthritis	1	1
asipro	1	1
bentonite clay	1	1
bethanechol	1	3
bile acid-binding resin	1	1
brain cancer	1	1
bulking agent	1	6
carbachol ophthalmic	1	1
carbamide peroxide	1	1
carbapenem antibiotic	1	1
chest x ray	1	1
chlorhexidine gluconate	1	2
cholinesterase inhibitor	1	2
chorionic gonadotropin intramuscular	1	5
claustrophobia	1	1
clorazepate dipotassium	1	2
competitive inhibitor of bacterial paba	1	1
compression stocking	1	1
control blood glucose level	1	2
creatine phosphokinase	1	2

cupric sulfate	1	1
darbepoetin alfa	1	1
desiccated ethyroid extract	1	3
dexpramipexole	1	2
digestive enzyme	1	3
diosmiplex	1	1
dopamine supplement	1	1
drug company	1	1
dystonia	1	1
eleutheroside	1	1
ethopropazine	1	1
exemestane	1	1
finesteride	1	1
fludrocortisone	1	1
folic acid	1	1
fondaparinux	1	2
fosfomycin tromethamine	1	2
galectin-3	1	1
general alcoholism	1	4
general antifungal	1	1
general antiviral	1	2
general colon	1	2
general diabete	1	1
general gout	1	2
general hypoglycemia	1	1
general joint health	1	1
general memory	1	2
general mood	1	1
general motion sicknes	1	3
general myasthenia gravi	1	1
general urinary control	1	1
gentian violet	1	2
glipizide	1	1
glucosamine hcl, chondroitin sulfate sodium, msm, hyaluronic acid	1	1
goserelin	1	1
gynecology	1	2
hearing aid	1	3

hepatiti b antiviral	1	4
high blood sugar control	1	2
human chorionic gonadotropin	1	1
human parathyroid hormone	1	4
hyperhomocysteinemia	1	1
igf 1	1	1
igfbp 3	1	1
insomnia	1	2
journal?	1	1
kinase inhibitor	1	3
lactobacillu bulgaricu	1	1
letrozole	1	1
levocarnitine	1	1
linagliptin	1	1
liotrix	1	1
lyme disease	1	1
mirabegron	1	2
modafinil	1	1
morphine	1	1
multiple possible item	1	2
mupirocin	1	1
naftifine	1	1
narcotic pain reliever	1	1
nefopam hydrochloride	1	1
neomycin	1	4
neuroprotection	1	1
neutropenia	1	1
nnrti	1	2
non-steroidal fertility medicine	1	1
nonsteroidal aromatase inhibitor	1	3
nootropic	1	5
ocular lubricant	1	5
opium tincture	1	1
pacemaker	1	3
paraneoplastic disorder	1	1
pathological laughter and crying	1	1
pcp treatment	1	2
peginterferon alfa 2a	1	1
peginterferon alfa-2a	1	1

peginterferon alpha 2b	1	1
peptide based formula	1	1
pharmaceutical company	1	2
phenazopyridine	1	1
phosphatidylserine supplement	1	1
phytosterol ester	1	2
picamilon	1	1
pneumococcal vaccine	1	1
polyphenol	1	4
pregnenolone	1	3
presurgery medication	1	1
qunidine	1	1
ramelteon	1	1
relaxing	1	2
restless leg syndrome	1	1
rimabotulinumtoxinb	1	3
rite aid	1	1
roflumilast	1	3
rosacea	1	1
scrotum medication	1	2
seborrheic dermatiti	1	1
selective irreversible mao b inhibitor	1	1
selective serotonin reuptake inhibitor	1	1
sequential compression device	1	1
sexually transmitted disease	1	1
skin antibiotic	1	1
skin bleach	1	7
sleep medication	1	3
small molecule kinase inhibitor	1	2
sodium chloride	1	1
stool softener and laxative	1	1
stres relief	1	1
sucalfate	1	1
testostorone	1	2
tetanu diphtheria vaccine	1	1
tinea cruri	1	1
tinea cruris	1	1

tolnaftate	1	3
ulcerative coliti	1	1
urinary tract antibiotic	1	1
urine test	1	3
vasculiti	1	1
vitamin b6	1	1

REFERENCES

- [1] Acary Souza Bulle Oliveira, R.D.B.P.; 2009; AMYOTROPHIC LATERAL SCLEROSIS (ALS): Three letters that change the people's life: Forever; Arq Neuropsiquiatr; 67; 3-A; 750-782;
- [2] Bulbar ALS. Available: <http://www.als.ca/sites/default/files/files/Bulbar%2520ALS.pdf>
- [3] Siân C. Barber, P.J.S.; 2010; Review Article: Oxidative stress in ALS: Key role in motor neuron injury and therapeutic target; Free Radical Biology & Medicine; 48; 629-641;
- [4] Siân C. Barber, R.J.M., Pamela J. Shaw; 2006; Review: Oxidative stress in ALS: A mechanism of neurodegeneration and a therapeutic target; Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease; 1762; 11-12; 1051-1067;
- [5] Jemeen Sreedharan, C.E.S.; 2009; The Genetics of Amyotrophic Lateral Sclerosis; ACNR; 9; 2; 10-16;
- [6] Alan E Renton, A.C.B.J.T.; 2014; State of play in amyotrophic lateral sclerosis genetics; Nature Neuroscience; 17; 17-23;
- [7] Le, S.C.S.Z.; 2013; Genetics of amyotrophic lateral sclerosis: an update; Molecular Neurodegeneration; 8; 28;
- [8] Bede P EM, Byrne S, Hardiman O. Sexual dimorphism in ALS: exploring gender-specific neuroimaging signatures. Amyotrophic Lateral Sclerosis & Frontotemporal Degeneration. 2014;15:235-43.
- [9] Coan, G., & Mitchell, C. S. (2015). An Assessment of Possible Neuropathology and Clinical Relationships in 46 Sporadic Amyotrophic Lateral Sclerosis Patient Autopsies. Neurodegenerative Diseases. PMID: 26183171
- [10] Webster, M. (2016) Crowdsouricng Definition.

- [11] Ball, P.; 2014; *Wisdom of the Crowd: The myths and the realities*; BBC;
- [12] Brabham, D.C.; 2013; *Crowdsourcing*; The MIT Press;vii-131;
- [13] Kitova, M.; 2015; *The Growing Trend Of Clinical Research Crowdsourcing*; Open Health News;
- [14] Darrow, J.J.; 2014; Article: *Crowdsourcing Clinical Trials*; Minnesota Law Review; 98; 805-876;
- [15] Allison B McCoy, A.W., Archana Laxmisan,Madelene J Ottosen, Jacob A McCoy, David Butten, Dean F Sittig; 2012; Development and evaluation of a crowdsourcing methodology for knowledge base construction: identifying relationships between clinical problems and medications; J Am Med Inform Assoc; 19; 713-718;
- [16] Orrell RW LR, Ross M. Antioxidants for treating amyotrophic lateral sclerosis. Cochrane Database Syst Rev. 2007.
- [17] Barber SC HA, Mead RJ, Barber S, Shaw PJ. An in vitro screening cascade to identify neuroprotective antioxidants in ALS. Free Radic Biol Med. 2009;46:1127-38.
- [18] Gianforcaro A HM. Vitamin D as a potential therapy in amyotrophic lateral sclerosis. CNS Neurosci Ther. 2014;20:101-11.10.1111/cns.12204.
- [19] Blasco H MHB, Defour0Rainfray D, Patin F, Maillot F, Beltran S, Gordon PH, Andres CR, Corcia P. Vitamin D is Not a Protective Factor in ALS. CNS Neurosci Ther. 2015;21:651-6.
- [20] Graf M ED, Horowski R, Kramer B, Riederer P, Gerlach M, Hager C, Ludolph AC, Becker G, Osterhage J, Jost WH, Schrank B, Stein C, Kostopulos P, Lubik S, Wekwerth K, Dengler R, Troeger M, Wuerz A, Hoge A, Schrader C, Schimke N, Krampfl K, Petri S, Zierz S, Eger K, Neudecker S, Traufeller K, Sievert M, Neundörfer B, Hecht M;

- German vitamin E/ALS Study Group. High dose vitamin E therapy in amyotrophic lateral sclerosis as add-on therapy to Riluzole: results of a placebo-controlled double-blind study. *J Neural Transm (Vienna)*. 2005;112:649-60.
- [21] Desnuelle C DM, Garrel C, Favier A. A double-blind, placebo-controlled randomized clinical trial of alpha-tocopherol (vitamin E) in the treatment of amyotrophic lateral sclerosis. ALS Rilutek-tocopherol Study Group. *Amyotrophic Lateral Sclerosis And Other Motor Neuron Disorders: Official Publication Of The World Federation Of Neurology, Research Group On Motor Neuron Diseases*. 2001;2:9-18.
- [22] Miquel E CA, Martínez-Palma L, Souza JM, Bolatto C, Rodríguez-Bottero S, Logan A, Smith RA, Murphy MP, Barbeito L, Radi R, Cassina P. Neuroprotective effects of the mitochondria-targeted antioxidant MitoQ in a model of inherited amyotrophic lateral sclerosis. *Free Radic Biol Med*. 2014;70:204-13.10.1016/j.freeradbiomed.2014.02.019.
- [23] Ashworth NL SL, Deforge D. Treatment for spasticity (muscle tightness and spasm) in people with amyotrophic lateral sclerosis/motor neuron disease. *Cochrane Database Syst Rev*. 2012.
- [24] A. J. Whitaker, "MEDICATIONS ALS PATIENTS TAKE IN THE LAST SIX MONTHS OF LIFE," Graduate Faculty of Department of Behavioral and Community Health Sciences Graduate School of Public Health in partial fulfillment of the requirements for the degree of Master of Public Health, 2003 2003.
- [25] H. F. o. America, "A Caregiver's Guide to the Dying Process," H. F. o. America, Ed., ed. https://hospicefoundation.org/hfa/media/Files/Hospice_TheDyingProcess_Docutech-READERSPREADS.pdf.

- [26] Staff MC. Diseases and Conditions Amyotrophic lateral sclerosis: Treatments and drugs2016. Available from: <http://www.mayoclinic.org/diseases-conditions/amyotrophic-lateral-sclerosis/basics/treatment/con-20024397>.
- [27] <http://www.webmd.com/brain/tc/amyotrophic-lateral-sclerosis-als-topic-overview#2>
- [28] Center UM. ALS treatment2016. Available from: <https://www.ucsfhealth.org/conditions/als/treatment.html>.
- [29] Kasarskis EJ BS, Vanderleest JG, Schneider AR, McClain CJ. Nutritional status of patients with amyotrophic lateral sclerosis: relation to the proximity of death. *Am J Clin Nutr.* 1996;63:130-7
- [30] Lacomblez L, Bensimon G, Leigh PN, Guillet P, Meininger V. Dose-ranging study of riluzole in amyotrophic lateral sclerosis. Amyotrophic Lateral Sclerosis/Riluzole Study Group II. *Lancet.* 1996;347(9013):1425-31.
- [31] Mitchell, C.S., Cates, A., Kim, R.B., Hollinger, S.K. (2015). Undergraduate Biocuration: Developing Tomorrow's Researchers While Mining Today's Data. *The Journal of Undergraduate Neuroscience Education* (JUNE), 14(1):A56-A65.
- [32] www.drugs.com
- [33] www.webmd.com
- [34] www.rxlist.com
- [35] Chao Chen AL, Leo Breiman. *Using Random Forest to Learn Imbalanced Data.* Berkeley.
- [36] Torsten Hothorn KH, Carolin Strobl, Achim Zeileis. *A Laboratory for Recursive Partytioning.* 2015.

- [37] Carolin Strobl A-LB, Achim Zeileis and Torsten Hothorn. Bias in random forest variable importance measures: Illustrations, sources and a solution. BMC Bioinformatics. 2007;8.10.1186/1471-2105-8-25.
- [38] R. L. K. Hung-Chia Chen, Kuang Fu Cheng and James J Chen, "Assessment of performance of survival prediction models for cancer prognosis," BMC Medical Research Methodology, vol. 12, 23 July 2012 2012.
- [39] C. S. a. A.-L. B. Silke Janitza, "An AUC-based Permutation Variable Importance Measure for Random Forests," BMC Bioinformatics, vol. 14, 2013.
- [40] ochen H Weishaupt CB, Esther Polking, Jenine Dietrich, Gundaula Rohde, Burkhard Poeggeler, Nina Mertens, Swetlana Sperling, Matthias Bohn, Gerald Huther, Armin Schneider, Alfred Bach, Anna-Leena Siren, Rudiger Hardeland, Mathias Bahr, Klaus-Armin Nave, Hannelore Ehreneh. Reduced Oxidative Damage in ALS by High-Dose Enteral Melatonin Treatment. Journal of Pineal Research. 2006;41(4):313-323.
- [41] A Chio EF, P Melneri, E Bottacchi, D Schiffer, and the ALS Percutaneous Endoscopic Gastrostomy Study Group. Safety and Factors Related to Survival After Percutaneous Endoscopic Gastrostomy in ALS. Neurology. 1999;53(5).
- [42] L Mazzini TC, M Zaccala, G Mora, M Del Piano, M Galante. Percutaneous Endoscopic Gastrostomy and Enteral Nutrition in Amyotrophic Lateral Sclerosis. Journal of Neurology. 1995;242(10):695-698.
- [43] Wayne M KM. Swallowing Disorder: Diagnosis and Therapy. Medical Clinics of North America. 1993;77(3):571-582.
- [44] G Marquardt VS. Use of intrathecal baclofen for treatment of spasticity in amyotrophic lateral sclerosis. J Neurol Neurosurg Psychiatry. 2002;72:275-276.

- [45] Jeong SY RK, Shultz K, Ponka P, Arosio P, David S. Dysregulation of Iron Homeostasis in the CNS Contributes to Disease Progression in a Mouse Model of Amyotrophic Lateral Sclerosis. *Nueroscience*. 2009;29(3):610-619.
- [46] Daniele Orsucci MM, Massimiliano Filosto, and Gabriele Siciliano. Tetracyclines and Neuromuscular Disorders. *Curr Neuroparmacol*. 2012;10(2).
- [47] Chalonda R. Handy CK, Nicholas Boulis, and Thais Federici. Review Article: Pain in Amyotrophic Lateral Sclerosis: A Neglected Aspect of Disease. *Neurology Research*
- [48] Hollinger, S. K., Okosun, I.S., Mitchell, C.S. (2016). "Antecedent Disease and Amyotrophic Lateral Sclerosis: What Is Protecting Whom?" *Front Neurol* 7: 47.
- [49] Mitchell, C. S., Hollinger, S. K., Goswami, S. D., Polak, M. A., Lee, R. H., & Glass, J. D. (2015). Antecedent Disease Is Less Prevalent in Amyotrophic Lateral Sclerosis. *Neurodegenerative Diseases*, 15(2), 109-113. PMID: 25720304
- [50] Irvin, C. W., Kim, R. B., & Mitchell, C. S. (2015). Seeking homeostasis: temporal trends in respiration, oxidation, and calcium in SOD1 G93A Amyotrophic Lateral Sclerosis mice. *Front Cell Neurosci*, 9, 248. PMID: 26190973
- [51] Robert Küffner, N.Z., Raquel Norel, Johann Hawe, David Schoenfeld, Liuxia Wang, Guang Li, Lilly Fang, Lester Mackey, Orla Hardiman, Merit Cudkowicz, Alexander Sherman, Gokhan Ertaylan, Moritz Grosse Wentrup, Torsten Hothorn, Jules van Ligtenberg, Jakob H Macke, Timm Meyer, Bernhard Schölkopf, Linh Tran, Rubio Vaughan, Gustavo Stolovitzky, & Melanie L Leitner; 2014; Crowdsourced analysis of clinical trial data to predict amyotrophic lateral sclerosis progression; *Nature Biotechnology*; 33; 51-57;

- [52] Norman, Thea. (2015) Prize4Life, Sage Bionetworks and DREAM Announce Winners of ALS Stratification Challenge. In Bionetworks, S. (ed.), Business Wire. A Berkshire Hathway Company, BusinessWire, Vol. 2016.